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A Case of Glioma of the Lower Cervical Region of the Spinal Cord Producing a Total Transverse Lesion, in which there was Spasticity of the Lower Limbs and Persistence of the Deep Reflexes.

I. A Study of the Tumor and Some of the Phenomena Produced Thereby. (presented)

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II. A Study of a Peculiar Form of Degeneration (Degeneratio Micans) Met with in this Case.

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III. Some Points in the Pathology of Syringomyelia.

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A CASE OF GLIOMA OF THE LOWER CERVICAL REGION OF THE SPINAL CORD PRODUCING A TOTAL TRANSVERSE LESION, IN WHICH THERE WAS SPASTICITY OF THE LOWER LIMBS AND PERSISTENCE OF THE DEEP REFLEXES.

I. A STUDY OF THE TUMOR AND SOME OF THE PHENOMENA PRODUCED THEREBY.

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II. A STUDY OF A PECULIAR FORM OF DEGENERATION (DEGENERATIO MICANS) MET WITH IN THIS CASE.

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III. SOME POINTS IN THE PATHOLOGY OF SYRINGOMYELIA.

By Simon Flexner, M.D.,
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I.

In August, 1890, Mr. W. C. T., white, aged fifty years, an intelligent and well-to-do farmer, consulted me on account of difficulty in walking and pain, which he located in his spine, from the upper dorsal region downward. He also complained of burning in both legs and feet.

His family history was good, no member of his family having died with tuberculosis or cancer. About six months before seeing me he had fallen off his horse backward, striking on his shoulders and neck. He attributed his sickness to this accident.

He was a well-nourished man, with no deformity of the spine and no well-marked point of local pain. He had no history of syphilis. His knee-jerks were considerably exaggerated, and he swayed markedly when standing with his eyes closed.

I gave him iodide of potassium in increasing doses and bichloride of mercury, which he took for about ten weeks, his condition, in the meantime, growing slowly and gradually worse.

In November, 1890, he passed out of my care, and the history of his illness from that time to December, 1896, I have obtained from the physicians who attended him and from the members of his family. During December, 1890, he had a severe attack of what his physicians called dysentery, and afterward his abdomen was greatly swollen for a long time. After this attack he was able to walk only with the aid of crutches. His bladder gave him trouble, and he also had more or less difficulty in evacuating his bowels. During the early part of 1891 a girdle sensation

developed, which was located somewhere in the region of the umbilicus. From the summer of 1891 until his death he was never able to walk even with the aid of crutches. During 1892–1894 he had several attacks of dysentery, and at these times passed pieces of the mucous membrane of the bowels. His abdomen much of the time was swollen. There was progressive paralysis of motion, the right leg becoming paralyzed some time before the left, and the patient thought that he had sensation longer in his left than in his right leg. I could get no reliable information as to where the paralysis of motion or sensation began. At times he used a catheter to draw his urine, but there appears to be no history of well-marked cystitis. His bowels usually moved every day or two, occasionally requiring the aid of an enema.

From the early part of 1895 to the summer of 1896 his general health, according to his statement, was excellent; his appetite was good; he was cheerful; did not suffer much pain and gained in flesh until he weighed nearly two hundred pounds. He had never at any time suffered the excruciating pain common to spinal tumors. At times, however, there was pain in the spine and a marked circle of pain around his body. This girdle of pain was always equally marked on both sides of the body, and slowly advanced upward until it reached a point above the nipples. All sensation and motion did not disappear until the latter part of 1895. The patient thought that after this time he could make no voluntary motion and feel nothing below the nipples.

He was troubled a great deal with what he called "jumping of the legs," the merest touch of the bedclothes frequently putting his legs to jumping, this "jumping" keeping up for some time. When bathing his feet the same trouble would be experienced, and he frequently kicked the tub over or splashed the water about.

During the period of his so-called good health he passed his urine at intervals of four or five hours, and his bowels moved every day or every other day, only occasionally requiring the aid of an enema.

His legs were more or less rigid, and at times there was a tendency to flexion; but for some time past they had remained straight and spastic, with the feet somewhat extended.

There had at no time been bed-sores.

There was one phenomenon about which he was very emphatic—the effect that strychnine, which was frequently given him, produced. Frequently during the course of his disease he suffered severely with burning in his body, legs, and feet. Strychnine invariably caused such increase of this burning and such increase in the "jumping" of his legs, though it caused no other inconvenience, that he refused to take it further.

In November, 1896, he made a visit to his daughter, who lived several miles away. While on this visit he was taken with vomiting, which he attributed to the eating of cheese. He returned home, and I saw him during the early days of December.

Notes taken at my first visit:

Patient is pale and greatly depressed in spirits. He has no fever, but his pulse is about 110 beats per minute. He is still vomiting occasionally, and says he can find no food which agrees with him. His abdomen is slightly swollen, but much less than it has been for a week past. His breathing is entirely diaphragmatic, and he suffers from

difficulty of breathing and a troublesome cough, which occasionally brings up a small quantity of frothy mucus. There is no rigidity of the back, and he usually suffers no great pain, but pain is produced when he turns his neck. In a darkened room his pupils appear smaller than normal, and they react indifferently to light. The palpebral fissures are somewhat narrowed.

Sensation. There is total absence of tactile, algesic, and thermic sensibility below the third rib in front and a little below the spine of the scapula behind, on the left side; on the right side the insensibility reaches a higher level. There is no dissociation of sensation at any point. Subjectively, there is some pain down his right arm and over the lower posterior portion of the neck when he turns his head. There is hyperalgesia over the top of the right shoulder and about both sides of the neck. All sensations are obtunded over the ulnar side of the right arm, forearm, and hand.

Trophic Changes. The legs are somewhat rigid, and their muscles appear firm and not wasted. The hip-joints, knee-joints, and ankle-joints are stiffened, but can be flexed, to some extent, by using force. The skin is not especially dry, scurfy, or glossy, and appears quite normal. There are no bed-sores, nor have there been any during the whole course of his sickness. The interossei between the little and ring fingers and between the ring and middle fingers of the right hand and the hypothenar eminence are somewhat atrophied.

Condition of the Reflexes. When the skin over any portion of his legs is pricked there is a motion of flexion. When the soles of his feet are tickled there is a motion in the toes and a tremor extends up the legs. When the toes are sharply lifted toward the knees a violent ankle-clonus begins, which lasts while the tension is kept up. The knee-jerks are well marked in both legs and considerably exaggerated in the left. I failed to elicit either the cremasteric or epigastric reflex. A digital examination of the rectum reveals the presence of well-marked contraction in the sphincter ani. (I did not insert a catheter into his bladder, and I was never able to get any of his urine for examination.) There is no deformity or rigidity of the spine, but over the upper dorsal region the percussion note is increased in resonance, and over the lower cervical region there is increase in dulness.

Diagnosis. A tumor of the spinal cord, probably intradural and, I fear, intramedullary, but on account of the persistence of the reflexes and the slow growth of the tumor I entertain the hope of operative relief should the patient gain sufficient strength.

The patient lived some distance from me, and during the next six weeks I only saw him four times, the last visit being made seven days before his death. At this time the reflexes were still present, but weaker. There was a bed-sore beginning behind the left great trochanter, and on the dorsal surface of the left foot there was a spot of roughly elevated, bluish skin, nearly as large as the palm of the hand, which had the appearance of a dried blister. During the last few days of his life his right arm was paralyzed to motion, and he suffered intense pain in both arms.

He died January 17, 1897. The exact cause of death I was not able to ascertain.

Four hours after death I was allowed to open only the spinal canal, as would have been done had an operation been performed.

The spinal cord, from the fourth cervical vertebra to the third dorsal vertebra, was removed. This portion of the cord is shown in Plate I. The upper five centimetres of the specimen—the part containing the enlarged tumor-formation—measured at the broadest point, laterally, 21 mm.; at the same point antero-posteriorly, 11 mm. The enlargement tapered gradually downward from the centre until, at the lower limit of the tumor, the measurements were about the same as those of a normal spinal cord. Immediately below the tumor, for about three centimetres, the cord was a softened mass; for a short distance it was not much larger than a small goose-quill, and bent of its own weight in any direction. The cord was placed at once into Müller's fluid, and on the next day was cut into sections about one centimetre long. The tumor was then plainly seen. It was a little darker in color than the cord, but both cord and tumor were stained with Müller's fluid, and the exact color of the tumor could not be made out. At some points the growth was about the consistency of normal spinal cord; at others, especially about the centre, the tissues were somewhat of a spongy appearance, while at other points cavities were plainly seen. The upper end of the specimen revealed two cone-shaped points, each situated in the region of the posterior horns of gray matter; these appeared to be the upper limit of the tumor. The first cut through the upper part of the specimen passed through an oblong, smooth-walled cavity measuring, laterally, 8 mm.; antero-posteriorly, 4 mm.; longitudinally, 5 mm. It contained the remains of a firm blood-clot the size of a small pea.

The third cut through the tumor, passing about its middle, revealed a lateral slit 10 mm. long. At this point the tumor appeared to occupy the entire cord, with only membranes surrounding it, which fell away from the sides of the tumor as the knife passed through.

The lower portion of the tumor presented an appearance of two cones lying side by side, with their apices jutting into the softened cord below. The softened cord appeared entirely disorganized, except the central stem of gliomatosis which passed through it. The lower limit of the specimen retained the normal, cord-like shape, with the central stem of gliomatosis occupying the position as indicated in Plate I.

Microscopical Examination. Section 1, Plate I. The lateral measurement of the cord at this point is 20 mm.; the antero-posterior, 11 mm. The anterior gray commissure has disappeared, and the tumor is plainly seen occupying a large portion of the cord. The mass of tumor extends right up to the direct pyramidal tracts, separated from them by a clear space and a few degenerated nerve-fibres only; these form a broken boundary running along the anterior border of the tumor. Nerve-fibres running in the same direction are seen here and there around the entire periphery of the tumor. To the left of the anterior commissure, just within the tumor mass, is a microscopical cavity of considerable length and of regular shape. This has a lining of cylindrical epithelium; at each end of the cavity the epithelium is irregular, and appears to have straggled from the line. The cavity is perhaps the remains of the normal central canal of the spinal cord. Anteriorly the rim of normal cord measures 2 mm., but it gradually becomes thinner posteriorly until all nerve-fibres disappear.

In the anterior rim of the cord many of the nerve-fibres are normal. The irregular outlines of the anterior horns of gray matter are also to be seen, with many ganglion cells, some of them more or less degen-

erated. Posteriorly the nerve-elements are more degenerated. The blood-vessels in the remnant of the cord and in the pia mater do not appear much changed. Conspicuous in the tumor is the great number of blood-vessels. Most of them, especially in the periphery, have immensely thickened walls, and in some instances the lumen is a mere slit or is even entirely obliterated. In some the vasa vasorum are yet to be seen. As the centre of the tumor—the region surrounding the main cavity—is reached there are found a few large, thin-walled bloodvessels (veins?) filled with blood-corpuscles. There are also in this locality numerous smaller vessels, with thick, homogeneous walls, many of which appear as solid rods.

Besides the bloodvessels the tumor is made up of cells and fibres. The cells are round, oval, and pyriform in shape, and in many places are arranged in a radial manner around the bloodvessels. They are most numerous in the periphery of the tumor, and toward the centre diminish in number. They are not, however, always regularly distributed, but are massed more abundantly in places and lessened in others. The fibres are also everywhere to be seen—fewest where the cells are most numerous, most where the cells are fewest. (For further description of the fibres and cells see Dr. Flexner's account.)

In Section 1 two cavities are to be seen—the larger centrally located, the smaller roughly S-shaped and located to the right. As the brink of the larger cavity is reached the cells become very much diminished in number, and the fibres are very abundant. Here and there this cavity is lined with cylindrical epithelium, and when this is the case these epithelial cells are nearly always reinforced by lines of cells immediately in their rear. Where there is no epithelial lining to the cavity the border is made up of neuroglia fibres, many of them projecting into the cavity in a very ragged manner. At various points around the edge of the cavity the glia fibres appear thickened and nodular. There are also many peculiar bodies; some are spindle-shaped, others horn-shaped, and some varicose, while others present small, nodular formations. Within this cavity there was a blood-clot as large as a small pea.

The surroundings of the smaller cavity differ from those of the larger, inasmuch as the cells around the smaller are fewer and the fibres and cells are much changed. There are also fragments of epithelial lining in this cavity, and here the epithelial lining cells are reinforced by cells immediately in their rear. The neuroglia fibres making up the border of this cavity show more marked changes than those forming the border of the larger cavity. Just behind this cavity the peculiar particles mentioned above are very numerous and strike the attention when the specimen is examined.

Section 2, Plate I This section is taken about 1 centimetre lower than Section 1, and measures 21 mm. laterally and 11 mm. antero-posteriorly. There is a continuation of the strip of cord which appears in Section 1. The anterior columns are to be seen, the anterior median fissure being displaced to the left. On the left a few ganglion cells are lying along the border of the tumor. The tumor has displaced the cord forward and outward until, posteriorly, all the nerve-elements have disappeared, and laterally they are very much degenerated, the strip of cord becoming thinner posteriorly until it disappears.

The tumor is very plainly circumscribed, and anteriorly and on the

side has a boundary of degenerated nerve-fibres running along its border. The structure of the tumor as to bloodvessels, cells, and fibres is entirely similar to that of Section 1. In the centre of the tumor is a cavity of irregular shape, filled here and there with fibres and a few cells, these being apparently the débris of the tumor as it appears in the immediate surroundings. There also appears here and there in the wall of the cavity and in the surrounding tissue broken lines of epithelial cells and some small, broken cavities with epithelial lining. In the immediate vicinity of this cavity bloodvessels (veins?) with thin walls, all filled with blood-corpuscles, are numerous. Many of these vessels are not round, but are irregular shaped—some as if two or three had been united and the partitions removed. The smaller arteries, with their slit-like or closed lumina, are also numerous. This cavity is evidently in a state of active formation. In the posterior border of the tumor there are several cavities, very irregular in shape, with a lining of exquisite cylindrical epithelium.

Section 3, Plate I (from a section one centimetre lower than Section 2.) Here the tumor reaches its greatest lateral measurement—21 mm., measuring antero-posteriorly 10 mm. The remains of the cord consist of a thin rim, less than 1 mm. thick in front and disappearing as the posterior border is approached. A few scattered ganglion cells are still to be found along the left anterior border of the tumor. The nerve-elements everywhere show marked degeneration. The cavity and its surroundings are very similar to those in Section 2. Here and there are fragments of cylindrical epithelium. The rod-like hyaline arteries are very numerous, and the thin-walled vessels (veins?) are filled with blood-corpuscles. *In places these thin-walled vessels have ruptured and the blood has been extravasated among the cells and fibres.* In the posterior region of the tumor there is a small, irregular cavity, lined here and there with a broken layer of epithelium. Near the centre of the posterior border there is a larger cavity, extremely irregular in shape, with thick-walled bloodvessels, standing upright, surrounded by radially arranged fibres and cells and covered by a beautiful layer of cylindrical epithelium. These formations stand out into the open space like Grecian columns, and present a very striking picture.

Section 4, Plate I (taken from about 1 centimetre below Section 3). At this point the tumor has a more rounded shape, measuring laterally 18 mm.; antero-posteriorly, 11 mm. The medullated nerves in the remnant of the cord are reduced on the left to a very small space on the anterior border, and on the right to a small space near the anterior fissure. There are no ganglion cells to be seen. Further out on either side, especially on the right, the degenerative changes are very marked. The structure of the tumor is the same as at the other points described. The conditions in the central cavity are also the same as in the other sections. On the left side there is a long, irregular cavity, which at some points has a lining of cylindrical epithelium, and is connected with the cavity by the disintegration of tissue. Posteriorly we have the same epithelium-lined cavity as described in Section 3, but the beautiful Grecian columns have lost their contour. Far to the right there is a roughly star-shaped cavity lined with cylindrical epithelium.

Section 5, Plate I (taken about 1 centimetre lower than Section 4). At this point the tumor and remnant of the cord measure laterally 15 mm.; antero-posteriorly, 9 mm. The thin rim of cord, thicker in front

than behind, more or less degenerated, extends nearly around the tumor, failing by a short space to connect dorsally. There are along the anterior border of the tumor a few degenerated ganglion cells to be seen. These do not appear to retain their processes. The nervous elements throughout the strip of cord appear much degenerated. The tumor at this point has undergone less degenerative changes than in any section heretofore described. There are no cavities which have had their origin in retrograde changes. Here also there are thin-walled vessels (veins?). The arteries with thickened walls are very numerous, and in nearly every case they show the radial arrangement of the cells and fibres; indeed, it is in this region of the tumor that this is most characteristically shown. It would appear that this radial arrangement of the cells and fibres is most commonly seen in that part of the tumor which yet preserves its natural structure, and must have existed around most or all of the arteries at some time in their growth. In that portion of the tumor which was between Sections 4 and 5 the preformed or epithelial-lined cavities were most numerous; at some places the structure of the tumor here might have been called cystic.

The tumor at the point from which Section 5 was taken showed very few signs of degeneration, although at several points around the epithelial-lined cavities the fibres are greatly increased over the cells, and these areas are paler than the other portions of the tumor.

Section 6, Plate I. This section was taken 1 centimetre below Section 5, and just a little way above the lower limit of the true tumor mass. Here the location of the apices of the tumor is seen, also the normally located central canal of the cord. The cavities contain epithelial lining and the remains of hemorrhages.

Below the true tumor for about 3 centimetres the cord, with the exception of the main stem of gliomatosis, was softened, the cord elements remaining as a mass of débris only. For a short distance below the true tumor, and apparently continuous with its two points, are two stems of gliomatosis, one soon disappearing, the other acquiring a central position and is continuous throughout the remainder of the removed portion of the cord. (Plate I.) In the main stem of the central gliomatosis, a short distance below the true tumor, there is situated well anteriorly and displaced to one side a deposit of cells, which is evidently the remains of the normally located central canal of the cord. The central area of gliomatosis in the softened part of the cord hardened well in Müller's fluid, and the fragments of the cord were held around it by the membranes.

Near the centre of the stem of gliomatosis, but distinctly separated from the original central canal, running from near one side to near the other side of the longest diameter of the stem, is a narrow slit, in some places not perfectly formed, in others an actual cavity, to be seen plainly with the unaided eye. In the stem of gliomatosis the bloodvessels are in striking contrast to the bloodvessels in the true tumor-growth. Their appearances in the true tumor have been described; in the area of gliomatosis they are not remarkably numerous, nor do their walls show any special changes. In the periphery of the area of gliomatosis the appearance is quite similar in all parts of the section; but as the centre is approached numerous bodies, which are to be described later, are to be seen. These bodies are located as seen in Fig. 2 and Fig. 3, Plate III. They present many different forms. Some of them are much

smaller than the unchanged cells making up the true tumor; some resemble thickened glia fibres (fibres in the sense of Weigert); some of them are larger than ganglion cells and are like them in many respects. They are round, oval, pyriform, club-shaped, nail-shaped, elongated, bulbous at one end, and gradually taper to a point not larger than the glia fibrils, being largest at the middle and tapering to a point at each end. They are screw-shaped, horn-shaped, twisted; many of them are varicose, and many, when stained, resemble granular tube-casts. These bodies are also to be found in the tumor proper, especially around the posterior border of the smaller cavity. (Fig. 1, Plate II.)

The most characteristic of these formations are not numerous at the very brink of the cavities (although some are seen lying free in the cavities, and many can be found making up the cavity walls), but just a little way removed. In some of the specimens examined they are not seen at the points where the cavities yet retain their epithelial lining.

From the resemblance that a few of these bodies have to ganglion cells I suspect that they have been mistaken for ganglion cells by some observers. Turner and Mackintosh (*Brain*, 1896, Parts II. and III.) describe a new growth with glia formation in the spinal cord. They give a photo-micrograph of a section containing a growth of glia, and in this they describe certain formations as most probably ganglion cells. The condition pictured by them is very similar to the condition existing in the stem of gliomatosis in the case here described, and I should think that the bodies which they have described as ganglion cells are the same as those present in my case. Turner and Mackintosh consider their case to be an example of the condition which has been described as *neuroglioma ganglionare*. Dr. W. Rosenthal (*Zeigler's Beiträge*, 1898, Band xxiii, Heft 1) describes a neuro-epithelioma of the spinal cord with central gliomatosis. He found and describes bodies similar in shape and location to those discovered in the case here presented. From an examination of some of Dr. Rosenthal's specimens, and from his description of the formations, I am of the opinion that the bodies found in his case and in mine are entirely similar in nature, although differing in size and shape. In a letter to me Dr. Rosenthal expresses the same opinion. I wish to thank him for sending me specimens from his case and for writing me his views of the peculiar formations. He is of the opinion that they represent a peculiar degeneration of the glia fibres (fibres in the sense of Weigert), and suggests the name "Kolbige Degeneration."

From a study of the bodies seen in my case I reached the opinion that some of them were changed and degenerating bloodvessels, and were, perhaps, some changed glia fibres (glia fibres in the sense of Weigert); but that a vast majority of them represented a degeneration existing in the bipolar cells, of ependymal type, which are found throughout the entire mass of the growth. I here merely wish to note also that though these bodies are not conspicuous as lining the cavities or making up the tissue which lines the cavities (though they may be found lying free in the cavities and many in the lining of the cavities), that they, or, rather the degeneration which is going on in them, do perhaps take some part—probably an important part—in the production of cavities, and especially of cavities which form in the new growth of glia. This statement receives some confirmation from the fact that these bodies are most numerous in the border of the smaller cavity (Plate II, Fig. 2). The tissue surrounding the smaller cavity in the figure just

mentioned is more of the nature of the tissue found in the stem of gliomatosis below the mass of the tumor than any other tissue to be found in the tumor proper. There are other cavities in the tumor proper which appear to have been produced by the hemorrhages from the thin-walled bloodvessels (veins?), the result being a disintegration of the cells and fibres which make up the tumor. The general lack of nutrition produced by the obliteration of the arteries also is, perhaps, an important factor in the production of these cavities. The existence of obliterating arteries and large, thin-walled vessels forming lakes of blood evidently produced a state of the blood-current which favored the disintegration of the central region of the tumor. Many cavities formed by the disintegration of tissue are connected with preformed epithelium-lined cavities, and it would be somewhat difficult to say in which process the cavity formation had its origin—that is, whether the cavity formation began first in the degeneration of the cells and fibres around the preformed cavities or in the disintegration of the tissues from nutritional changes.

After studying for awhile the peculiar degeneration in the tumor elements, which I have described in a very superficial way, I came to the conclusion that the subject was of sufficient importance to demand the hand of an expert, and after consultation with Dr. William H. Welch, Dr. Lewellys F. Barker kindly did the work, an account of which is here appended, and for which I am very grateful. I wish especially to thank Dr. Simon Flexner for many kindnesses and his contribution, which has been in my hands for several months. Also I wish to say that my study of the degeneration in the glia-elements was made during the summer of 1897, several months before the publication of Rosenthal's paper. I desire to thank Mr. Max Brödel, the artist, for his interest in the work and his excellent drawings, which have been well reproduced by the heliotype process.

Origin of the Tumor. It will be observed that in the history here reported the patient attributed the disease to trauma—*i. e.*, falling backward off his horse. He had been in perfect health up to the time of this accident, and only a short time—a few weeks—afterward he noticed the first symptoms of spinal-cord disease. He was conscious, however, from the time of the fall that his back was injured in the lower cervical region.

In other cases of tumor formation in the spinal cord there has been history of trauma; and it is quite probable that injuries may start into activity the latent embryonic elements from which these pathological formations have their origin.

For further details of the histology and histogenesis of the condition I refer to Dr. Flexner's account.

As the patient whose case is here reported came into my hands for surgical aid, a few words on the surgical aspect will not be amiss.

Starting with the assumption that spinal-cord tumors (I here exclude

tubercular and syphilitic neoplasms) offer no hope of relief through any other therapeutic means, they appeal alone to the aid of surgery. Tumors of the spinal cord are rapidly and surely fatal, and when, according to the cases collected by Starr, such a large per cent. can be reached and removed by the surgeon, it becomes our imperative duty to furnish these unfortunate sufferers with all the relief that surgery affords; but here I do not refer, of course, to intramedullary tumors, for one could hardly conceive of the successful removal of a tumor so placed, but a circumscribed intramedullary tumor may yet become of interest to the surgeon in other ways than from a purely diagnostic point of view. It is evident that in exceptional cases, either from lack of accurate history of the case or from symptoms so nearly alike in each condition, there may be great difficulty in deciding, even with a reasonable degree of certainty, whether the tumor is intramedullary or extramedullary. Fortunately for the surgery of the spinal cord, which was so brilliantly inaugurated by the case of Gowers and Horsley, these mystifying cases of intramedullary tumors are not very frequent.

Operations have been performed not intentionally (as would likely have been done in the case here reported had the patient's strength permitted) in cases of intramedullary growth. Some of these operations are not to be regretted either by the unfortunate sufferers or the surgeons; for as long as it is justifiable to prolong life and lessen suffering, even in hopeless cases, any reasonable therapeutic agent is advisable.

It should be borne in mind that in many of the cases of intramedullary tumors belonging to the class of the one here reported the destruction of the nerve-fibres is a slow process, and would probably be rendered much slower but for the resistance made by the encompassing bony walls of the spinal canal.

Operation for relief of intracranial pressure in tumors of the brain is not only justifiable, but in some cases is even attended with a wonderful improvement of the general condition of the patient; and not only do the symptoms produced by the pressure disappear, but there may be a recession of the growth itself.

Naturally the anatomical and physiological, and even the mechanical, conditions existing in the spinal cord and its envelopes—membranous and bony—are different in many respects from these conditions as they exist in the brain.

Bearing in mind the absolute necessity for the integrity of the conducting fibres in the spinal cord and the rôle played by the bony canal in the destruction of these fibres in intramedullary growths (gliomata), it is not difficult to conceive of cases when life may be prolonged and made more comfortable by an operation done solely to relieve pressure.

Then, when the diagnosis is impossible between an intramedullary

and an extramedullary tumor, the rule should be to operate; and when there is reasonable certainty that the growth is intramedullary and circumscribed, and that the relief of pressure would prolong and make life more endurable, I see no reason why an operation for the relief of the pressure (thus preserving for awhile longer fibres in the spinal cord) would not be quite as justifiable as an operation made to relieve intracranial pressure and its attending devastations.

The Reflexes. From a careful examination of the tumor and the softened cord below there can be no doubt as to the lesions having produced a total transverse division of the cord; and this destruction of continuity must have occurred at least some months before the death of the patient.

Until within the last few years it was considered a well-established fact in the pathology of the nervous system that total transverse lesions of the spinal cord above the lumbar region, where the lumbar enlargement was not implicated, produced an increase of the deep reflexes of the lower limbs and a spastic condition of the same.

Sir William Gowers still holds to his opinion, and in the last edition of his authoritative work, *Diseases of the Nervous System*, in reference to those cases in which the deep reflexes are lost, says the following: "A few cases have been met with in which a transverse lesion of the dorsal cord, especially a transverse concussion-myelitis, without post-mortem signs of lumbar inflammation, has caused a persistent loss of reflex action in the legs. In these cases, however, there has been not only loss of the muscle-reflex action, but also of the skin reflexes—a clear indication of an exceptional condition. Moreover, there has also been loss of faradic irritability and rapid muscular wasting—in short, there have been all the indications of a lumbar myelitis. The most probable explanation of these cases is that the descending degeneration of the pyramidal tract has been more than usually irritative in nature, so as practically to amount to a parenchymatous inflammation, and that this has invaded the motor structures as a nutritional change sufficient to abolish their function without, however, destroying their form. In one such case it was noted that the lumbar nerve-elements were extremely granular in aspect."[1]

Byrom Bramwell, in the latest edition of his able work, *Diseases of*

[1] From a letter to the author dated April 1, 1898:

"Yes, I hold the same views regarding the effect of a transverse lesion on the knee-jerk—that there is no interference of a lasting character unless true inflammation descends the cord or occurs independently in the lumbar enlargement. It is important to remember that it may spread down the cord in the posterior region alone, and this may arrest the reflex action. The cases are distinct in which evidence of the occurrence on such secondary inflammation has coincided with loss of the knee-jerk, while the experimental and other evidence that a simple transverse lesion does not cause such loss is quite conclusive. Indeed, a single case of the loss shows that, when met with, it must be due to some additional element beyond those of a simple transverse lesion.—W. R. Gowers."

the Spinal Cord, says: "Within the last few years it has been stated that if you completely remove the control of the brain from the reflex centres in the spinal cord, instead of producing exaggeration you produce abolition of the deep reflexes." Dr. Charlton Bastian, who advances this view, states that when the spinal cord is crushed and completely destroyed in the dorsal region (when, for example, its whole thickness is absolutely destroyed by a transverse myelitis) the deep reflexes in the lower limbs are completely and permanently abolished, even though the lumbar enlargement is not directly implicated by the lesion. He maintains that when the lesion completely severs the connection between the brain and the lower part of the spinal cord the reflexes in the portions of the cord below the lesion are permanently abolished. With Dr. Hughlings-Jackson he believes that the cerebellum exerts an enforcing influence upon the lower (spinal) reflexes. Dr. Hughlings-Jackson and other good observers have published cases in support of this view, which was generally accepted only a few years ago.

"But whether Dr. Charlton Bastian's view is correct or not—and I must say that, speaking for myself, I have not met with any cases which support it—lesions which involve the crossed pyramidal tracts are, in the vast majority of cases, attended with exaggeration of the deep reflexes."

Holt and Herter (*The American Journal of the Medical Sciences*, April, 1895), in referring to a case in which they considered, that there was a total transverse lesion of the cord, say: "The analgesia below the neck, the spasm of the legs, and the heightened reflexes are, of course, merely the usual results of a total transverse lesion of the cord in the cervical region."

It would be useless to go further, for up to the time of Dr. Bastian's later contribution (*Medico-Chirurgical Transactions*, 1890) it was generally held by all authorities that a total transverse lesion in the cervical or upper dorsal portion of the spinal cord, unattended with degeneration of the lumbar enlargement, produced an increase in the deep reflexes and spasticity in the legs. Notwithstanding the fact that this position was generally held, a review of the cases reported in the literature at my command furnishes very meagre evidence in support of this hypothesis.

Dr. Bastian's views caused a general revision of the whole subject; so that at present it would appear that his position is the one accepted by a large majority of the observers.

E. S. Reynolds, "On the Condition of the Reflexes in Total Transverse Division of the Spinal Cord" (*Brain*, spring, 1895), reviews the subject very carefully, and finds that such authorities as Bowlby, Thorburn, Bruns, and many others equally noteworthy, agree in the main

with the views promulgated by Dr. Bastian, and reaches the following conclusion: "From the above observations we must see that after total transverse division of the cervical or upper dorsal region of the cord there almost *always* (italics mine) results a lasting loss of the deep reflexes of the legs, with flaccid paralysis of the muscles, and at the same time there may be no marked atrophy of muscles, no great alteration of the electrical reactions, and no affection of the gray matter in the lower dorsal and lumbar regions. No satisfactory explanation of the phenomena observed is as yet forthcoming, the cerebellar theory put forward by Bastian being perhaps the most feasible.

"More observations are yet necessary before this subject, which affects one of the most fundamental principles in neurology, can be satisfactorily settled."

Kocher, in his recent and very able work on *Injuries of the Spinal Cord*, is very positive that the deep reflexes are lost when the cord has sustained a total transverse division.

The symptoms in a case of my own, in which there was a total transverse destruction of the cord from a fracture of the body of the fifth cervical vertebra, reported in the *Journal of Nervous and Mental Diseases*, June, 1897, agree with the views of Bastian, Kocher, and others mentioned.

D. Gerhardt (*Deutsch. Zeitsch. für Nervenheilkunde*, 1894, Band vi., pp. 127–136) reports a case which he thinks opposes the views of Bastian, and points out the fact that if one case of undoubted transverse division of the cord can be furnished in which the reflexes remain, Bastian's cerebellar hypothesis will be overthrown.

Reynolds, who abstracted the report for *Brain*, thinks the case not conclusive, as there may have been, while the reflexes lasted, still a small portion of gray matter connecting the cord.

A case reported by Bruns (*Archiv für Psychiatrie*, vol. xxv. pp. 1–72), in which there was a total transverse lesion of the spinal cord between the last cervical and first dorsal vertebræ, shows beyond question that the position taken by Gowers in the quotation given in this article is not supported in its entirety by the facts in many cases. In Bruns' case there was not sufficient degeneration in the peripheral nerves or in the muscles to account for the absence of the deep reflexes, and the lumbar enlargement was, with the exception of the descending degeneration of the pyramidal tracts, healthy to the most reliable methods of examination.

I single out the case of Bruns because it is considered the strongest proof yet given that a total transverse lesion would *always* produce abolition of the deep reflexes and flaccid paralysis of the lower limbs, *without* there being present degeneration in the lumbar enlargement or the peripheral nerves or the muscles.

Many other cases of total transverse lesions show the presence of the superficial reflexes and faradic irritability; so the views of Dr. Gowers, while correct in some essential parts, must be modified.

In my case it is to be deplored that a more extensive examination of the spinal cord could not be made; but, from the positive nature of the symptoms, it is really only necessary to establish the fact of the complete severance of the cord by the tumor to make the case one of conclusive evidence.

It should be borne in mind that most of the cases which have been presented as proof that a total transverse lesion of the spinal cord destroys the deep reflexes in the lower extremity, and produces a flaccid paralysis of the same, have been traumatic injuries, in which, at the same time that the cord is crushed, there are also produced violent circulatory and dynamic changes in that portion of the cord below the injury. In disease-conditions not dependent on traumatism, irritative and other forces are at work which must greatly influence the spinal cord.

The case I have reported here furnishes conclusive proof that in certain conditions the spinal cord may be completely severed and yet the deep reflexes remain.

The process by which the division of the cord is effected and the attending changes in the cord below the lesion are probably the conditions which cause the reflexes to be retained or abolished.

In my case the tumor was one of very slow growth, extending over nearly seven years. It did not infiltrate the cord immediately around it, and must have destroyed its continuity in such a way as to produce the very least possible irritative and circulatory changes in the lumbar enlargement.

In a case to be reported by me in the future, of a large cerebellar cyst which was evacuated with recovery of the patient, I offer some evidence which might be used against the cerebellar hypothesis of Bastian. In this case the deep reflexes were totally absent, and had been for some time; but very soon after the evacuation of the cyst, which had destroyed by excavation and pressure much of the cerebellum, the reflexes returned and the knee-jerks were considerably exaggerated. This return of the knee-jerks occurred long before there was any indication whatever that the cerebellum was resuming its functions, and when the cerebellum was more nearly completely destroyed than in any other case heretofore reported in which there was recovery. The destruction of the cerebellum and the attending increase of the knee-jerk coincide very closely with the results obtained by Ferrier after the removal of the cerebellum in monkeys.

It should also be remembered that cases have been reported in which the lesion did not produce a total transverse division, and yet the deep reflexes were lost.

Without attempting to account for the loss of the deep reflexes in lesions of the basic ganglia and in the exceptional cases of lesions of the pre-frontal lobes and of the cerebellum, beyond attributing the loss to the general irritative and inhibitory influences which the lesions exert over the entire cerebro-spinal system, I have the following conclusions to offer:

That the cord may be intact and lumbar degeneration, or degeneration in the peripheral nerves or muscles, may be absent, and yet there may be absence of the deep reflexes.

That the cerebellum in the human subject may be largely destroyed and the remaining portion functionally inactive, and there may still be an increase in the deep reflexes in the lower limbs.

That the spinal cord may be totally severed in the upper dorsal region and still increase in the deep reflexes, and spasticity in the lower limbs may be present.

That the rigidity of the paralyzed limbs is not due, as Dr. Bastian terms it, to the "unrestrained," or, as Dr. Hughlings-Jackson terms it, "unantagonized," influence of the cerebellum passing downward to the spinal cord.

That the spinal cord is the centre for the deep reflexes, and has also within itself the power of producing spasticity of the muscles.

(I am not prepared to say, however, that the spinal cord has not the power, when conditions are favorable—for the transference of power in other parts of the body and brain is well known—of centering in itself functions which are normally distributed throughout the entire cerebro-spinal system.)

From the foregoing evidence it would appear that the deep reflexes are dependent on some power in the spinal cord which severe "shock," such as injuries and violent disease processes, destroy, not for a few days only, but in many cases for all time; and that the loss of the deep reflexes is produced by other causes than the total division of the cord cutting off the normal influences of the cerebellum or cerebrum, or both.

II.

A STUDY OF A PECULIAR FORM OF DEGENERATION (DEGENERATIO MICANS) FOUND IN THIS CASE.

EXAMINATION OF UNSTAINED SECTIONS IN WATER AND IN SALTY GLYCERIN.

Around the slit-like cavity in the centre of the tumor mass one can in unstained sections, even with the naked eye, see that there exists a band of variable thickness somewhat more opaque than the rest of the tumor.

With a magnification of 10 diameters (Plate III. Fig. 2) it is easy to make out that this opacity is due to the presence in the tissues in this area of minute, irregular particles and rods that look dark on a much lighter-colored background, the latter resembling in appearance the main mass of the tumor. With this magnification it is evident that (in the section examined) these dark particles are not evenly distributed about the slit-like cavity, but are much more numerous in the tissue on one side. Even on this side the area in which the bodies are very numerous is not of equal width in all places, being from three to four times as broad at one extremity of the slit as at the other, while in the areas in which the bodies occur there is considerable variability in the number of particles present. There is no marked grouping of the particles nor is there any sharp line of demarcation between the tissue in which they occur and the main mass of the tumor; at the periphery of the band the particles are numerous; they grow rapidly fewer in number until the band with dark particles and pale background goes over into the main tumor mass, consisting entirely or almost entirely of pale background. The background of the band containing the particles is, however, on the whole, a little paler than the main mass of the tumor, which, again, is not entirely free from the dark particles. Here and there single particles can be made out in different parts of it.

With the magnification of 62 diameters (Zeiss apochr. obj. 16 mm. compens. oc. 4) one can make out that the dark particles noticeable at 10 diameters now look dark yellow or yellowish-brown (Müller's fluid hardening), while the pale background looks almost colorless or has at most a feeble straw-colored tint. Some of the yellow masses are now recognizable as bloodvessels, cut longitudinally, transversely, and obliquely, filled or partly filled with fairly well-preserved blood, the individual corpuscles of yellow color being distinctly visible with this magnification in some of the vessels. (Plate III. Fig. 3.) By far the majority of the particles are evidently not bloodvessels, however; they are, on the whole, smaller, more refractive, more solid, and much more irregular in size and shape. In size they vary from particles smaller than a red corpuscle to masses 0.1 mm. and 0.2 mm. in length and 0.05 mm. to 0.02 mm. in breadth. Very frequently the large masses are thin at one end and thick at the other. They may be straight or may form stiff curves. In large part the variable form is evidently due to the fact that long masses running in almost every direction through the tissue are met with in the section sometimes cut parallel to the long axis, sometimes transversely to this axis, or, again, in every degree of obliquity.

Many of the small and some of the larger masses look to be homogeneous, or nearly so, in this unstained preparation. The majority of the larger masses, however, present a moniliform or twisted appearance.

The latter, when it occurs in a long, tapering body, thick at one end and thin at the other, strongly suggests a screw in shape. Again, a long, curved body, with one delicate extremity and another broad extremity, may closely resemble in shape and appearance a brass horn.

With this magnification, what was described above as pale background is seen to be far from homogeneous. It consists of (1) longer and shorter interwoven rods, fibres, or spindle-shaped bodies; (2) small, rather spherical, but less regular masses, which resemble cell-bodies; and (3) a somewhat granular, ground substance that presents the appearance of a precipitated albuminous fluid.

With a magnification of 500 diameters (Zeiss apochr. obj. 2.0 mm., compens. oc. 4) the details of the structure become much clearer. Leaving the peculiar bodies or particles temporarily out of consideration, the tissue about the cavity is seen to be made up of a mass of cells and fibres embedded in a granular material which evidently represents the precipitated particles of an albuminous fluid. The elements composing the tumor are here enormously swollen and loosened, as though they had been exposed to the action of some macerating or dissociating fluid. The study of the unstained elements making up the mass is facilitated by mounting in salty glycerin. The main constituents are found to be longer and shorter, narrower, and broader, spindle-shaped fibres, containing elongated vesicular nuclei, the latter being situated usually, though apparently not always, at the broadest part of the fibre, and generally eccentrically, sometimes at the very margin of the cell. Portions of two such cells are illustrated in Plate III., Fig. 4, *a*.

These fibres, then, are in reality the protoplasm of much elongated bipolar cells. A number of structures looking like round-cells, each with a small, round nucleus placed eccentrically, are met with in the section. These, in all probability, are correctly considered to be transverse sections of the elongated cells or fibres, the sections happening to pass through a part of the cell in which the nucleus is situated. There are an enormous number of small round, oval, or polyhedral bodies, which vary in size from minute dots as large as the granules of an eosinophilous leucocyte to large masses 20, 40, and more microns across. These apparently represent cross sections of fibres of different thicknesses cut at various distances from the nucleus. One can scarcely ever follow one of the long cells throughout its whole course, for the fibres are so interwoven, twisted, and curved that each leaves the section at some part of its course. Accordingly, what one sees is a complex feltwork of longer and shorter segments of cells, some of them containing nuclei, others, of course, being devoid of nuclei on account of the plane of the section. It is possible that not all of the fine fibrils are really processes of bipolar cells. Some of them may be glia fibres, in Weigert's use of the term, since occasionally several can be seen passing through the

protoplasm of a single spherical cell. That the processes of some of the bipolar cells may be almost if not quite as delicate as these glia fibres is, however, certain, and there are all transitions in thickness from these fine fibrils to the large, clear, enormously swollen fibres. Just how many of the fibrils represent Weigert's glia fibrils, and how many are the processes of delicate bipolar cells, cannot be determined.

It can be made out with this magnification that the particles or masses which were distinguishable, even with a magnification of 10 diameters, are in large part situated within the swollen bipolar cells, sometimes involving only a portion of the cell-body, in other instances apparently representing a transformation of the whole mass of the protoplasm of the fibre, at least for a portion of its extent. These particles or masses as seen in sections in salty glycerin are for the most part of a yellower color than the rest of the tissue (even much yellower than the corpuscles in the bloodvessels), and are highly refractive. These masses seldom look entirely homogeneous. On the contrary, they seem to consist of clumps or strands of a waxy-looking substance. They may be entirely separate from one another or partially fused with one another, or a number may be entirely fused to form a rather large, almost homogeneous mass of the substance. In the screw-shaped or horn-shaped masses the clumps or strands tend to be more isolated at the narrow end of the screw or horn, while at the broader end they are usually fused (or, to be more objective, at the broad end it is often impossible to make out that the substance is made up of smaller masses). The long masses often exhibit irregular, varicose enlargements in their course. In places the fused masses resemble very closely fused and altered blood, but with care no mistake on this point is likely to be made, as the blood in the capillaries is less refractive and more granular. Besides, in some instances the refractive masses occupy only a small portion of the protoplasm of the bipolar cell or fibre, and accordingly could have no relation to blood unless one made the improbable assumption of a phagocytosis of extravasated blood by the bipolar cells.

In many of the long cells cut parallel or nearly parallel to their long axis the refractive masses are obviously arranged in the form of parallel rows, as though they had resulted from a transformation of longitudinal fibres or longitudinal areas in the protoplasm. These longitudinal, parallel masses may be extremely fine and delicate or may be coarse. Not infrequently they are visible in the periphery of the cell, sometimes apparently on the surface of it, sometimes scattered through a part of its substance.

The longitudinal masses, as a rule, do not extend far without interruption, though occasionally they can be followed for a distance of from 15 to 20 microns. Usually they are very frequently interrupted, and resemble, then, minute beads of refractive substance arranged in rows.

The larger minute masses often look fusiform or spindle-like in shape, and when lying on the surface of a tapering cell-process in numbers remind one strikingly of the gross morphological appearance presented by masses of tigroid in the dendrite stained by the method of Nissl. Only in gross form and distribution, however, does the resemblance hold, for the spindle-shaped masses are yellow or of a straw tint, and, as a rule, they are not granular, but homogeneous and translucent. The large masses of the refractive substance are often continuous at one extremity, with multiple longitudinal bands or multiple rows of droplets or spindles of the substance. Sometimes an oblique cut through a large mass of the material reveals only partial fusion, and one sees projecting from the cut extremity a number of nodular masses arranged in rows projecting from a more solid mass, reminding one in form of the nodulated, fleshy stems of a cactus.

In a large number of instances the refractive masses seem to occupy the whole area corresponding to the body of the bipolar cell. Where this is not the case the protoplasm not involved is easily distinguishable from the rest of the mass, being less yellow and less refractive and sometimes finely fibrillated or granular. As a rule, however, it is of a slightly straw-colored tint, and more refractive than the protoplasm of the majority of the swollen bipolar cells, which do not contain the peculiar masses. One gets the impression that there are many transition stages from the pale feeble refractive protoplasm of the least altered bipolar cells to the yellowish, highly refractive protoplasm of the cells which contain the peculiar masses described. Again, the color and refraction of the peculiar masses themselves vary a great deal; whereas, the larger masses are very yellow and highly refractive (Müller's fluid, section unstained, examined in salty glycerin). The minute strings, droplets, or spindles of the substance are often only feebly straw-colored and of lower refractive power. Large, swollen, refractive bipolar cells occur which are entirely devoid of the peculiar substance: others contain only a few strands at the periphery or in the substance of the cell protoplasm.

In some of the cells the periphery of the small refractive masses appears to be fragmented and flake-like in appearance.

Outside of the large bipolar cells there can be made out large numbers of minute fusiform or moniliform masses of the substance precisely similar in appearance to those which tend to run parallel to one another inside the cells. It is extremely difficult to say whether these represent totally transformed bodies of delicate bipolar cells or are altered glia fibres in the sense of Weigert. One could easily be tempted to form the hypothesis that the masses both inside and outside the bipolar cells are altered Weigert's glia fibres; but while a certain number of bipolar cells contain within their protoplasm what appear to be unaltered glia

fibres, in the majority it is impossible to see such fibres, and in many it is difficult to discern even any trace of a longitudinal fibrillation. Again, in many of the large, spindle-shaped cells, as has been mentioned above, the whole mass of protoplasm seems to be replaced by the peculiar refractive substance. At present, therefore, a simple objective description seems more desirable than the making of hypothetical explanations.

In many of the bipolar cells the nucleus has undergone a marked swelling, accompanied by extreme vacuolization, but no definite relation, at least in the unstained preparation, between the nucleus and the peculiar masses has thus far been established.

Action of Reagents upon the Peculiar Masses in Celloidin Sections. (*a*) *Water* has no effect on the bodies in a celloidin section.

(*b*) *Nitric acid* in concentrated solutions rapidly removes the yellow color from the masses as well as from the rest of the tissue, but in other respects they are very resistant to the prolonged action of the cold acid. With hot nitric acid they disappear, but not before the rest of the new growth.

(*c*) *Caustic Potash.* A 10 per cent. solution of KOH swells the masses very slightly, if at all, and the form is still easily recognizable after action for several hours. They are even very resistant to hot KOH (10 per cent.), appearing longer than the other elements of the tumor. Finally, however, they swell up, dissolve, and disappear from view. This test easily distinguishes them from myelin. In the first place the resistance of myelin sheaths to the potash is much greater than that of these masses, and, further, while the myelin sheath becomes more refractive in the hot KOH, the peculiar bodies in the bipolar cells lose their refractiveness and become dull looking.

Many of the cells of the tumor contain in their protoplasm large numbers of minute granules a little smaller than eosinophilic granules. These are very resistant to hot KOH, and, on account of their persistence and high refractive power, are striking features on high-power examination of a specimen thus treated.

(*d*) *Lugol's solution.* The masses stain brownish or reddish-brown. On addition of 25 per cent. sulphuric acid the color is not much changed, although the bodies assume, perhaps, a somewhat deeper reddish-brown tint.

Study of Stained Preparations. *Weigert-Pal staining* (Plate III. Fig. 4). In sections stained by this method a large proportion of the very refractive masses stain black. If the differentiation be pushed the tint may become brownish or even yellowish-brown in some of the finer particles of the substance; but with ordinary staining all the particles, both large and small, stain jet black. The tint assumed is strikingly different from that presented by the stained myelin of medullated nerve-

fibres, the latter, as is well known, staining of a distinctly bluish-black tint. Even with very low magnification (10 diameters), the black, stained masses stand out prominently on a yellowish background formed by the rest of the tumor.

With higher magnification (62 diameters) the same curiously shaped masses (in the form of rods, flasks, screws, and horns) can be made out, as have been described in the unstained preparation. Here all are stained black. In some instances at the edges of the black masses can be seen yellowish refractive borders, corresponding to the protoplasm of the fibres, in which the black masses are situated. Here and there quite large, refractive yellow masses, with a tendency toward a spherical or oval shape in the sections can be seen, containing scattered through them larger and smaller amounts of the substance, which stains black. The blood in the bloodvessels and the extravasated blood in the tissues stain very differently from the refractive substance under consideration, and there is no trouble in differentiating between the two. For the details of the structure, however, higher powers and eventually oil immersion lenses must be employed. A magnification of 500 diameters (comp. oc. 4, apochr. obj. 2.0 mm.) suffices to make nearly all the relations clear. In specimens so studied it is clear that nearly all, if not all, of the very refractive yellow substance seen in the unstained preparation stains jet black or brownish-black in Weigert-Pal. As before described, this substance appears under various conditions; in solid, non-analyzable masses (Fig. 4, *b*), and in particles, droplets (Fig. 4, *o*), rods, and spindles (Fig. 4, *g*), of varying size and distribution, being almost without exception inside the bodies of the bipolar cells. Very often the droplets, rods, or spindles are arranged in rows (Fig. 4, *c*, *d*, *e*, *f*, *h*) upon or near the surface of the cells or within the substance, and one gains the impression that the type arrangement is fibrillary, the curious relations met with resulting from granular breaking up of the fibrils, with lesser or greater fusion of the broken-up parts, the fusion occurring in either a longitudinal or a horizontal direction in the cells. Occasionally one of the rows of rods, dots, or spindles takes a tortuous course inside the straighter process of a bipolar cell, and may even form a spiral inside the protoplasm of the latter. Sometimes running among the cells of the growth one can see very fine fibrils, which in ordinary gray matter would probably be taken to be glia fibrils which have undergone partial or total change into the refractile, black-staining substance (Fig. 4, *n*). Some of these fibrils look intensely black, as though consisting of a homogeneous black substance; others appear to be made up of a row of irregularly sized granules or droplets of the black substance, separated from one another by pale, yellowish interspaces. Other fibrils nearby may he unaltered, consisting of feebly yellow-colored homogeneous protoplasms. In the large wedge-shaped

or conical masses the broad end often stains uniformly black, while at the narrow end the black substance resolves itself into more or less parallel rows of black or brownish-black rods, dots, or spindles. Occasionally the smaller fragments can still be recognized through the whole of one of the larger bodies. When a fibre (*i. e.*, process of a long, thick, bipolar cell) running lengthwise in the section is cut somewhat obliquely through its broad extremity one can see the homogeneous mass of black substance projecting from the cut end. (Fig. 4, *o*.) Sometimes it occupies the whole cross-section of the fibre in its broad part; at other times it is surrounded by a peripheral area of protoplasm which has not been transformed, but which looks more refractive, as a rule, than that of adjacent cells. (Fig. 4, *e*.) Sometimes this protoplasm or unblackened part of the cross-section of the fibre consists of two sorts of substance: a peripheral, more refractive substance, and an internal, more pale and less refractive substance. In this paler substance are often situated smaller fragments of the black substance seen in cross-section. Entirely corresponding appearances are met with in longitudinal section through cells altered in the same way.

From the study of numerous places in the sections one gets the impression that the large spherical or oval bodies met with may represent areas in which the protoplasm of the fibres has "run" into a large mass of the substance, for in these masses one can see black dots, rods, or spindles, arranged in various ways (Fig. 4, *k*); sometimes in spirals, sometimes in more or less concentric rows, sometimes irregularly distributed. It is possible that the appearance may occasionally be due to the coiling up of the whole fibre, with apparent fusion of the coiled-up parts; more often it looks as though the substance of the fibre had "run" to collect in the larger mass, and so to form a huge, varicose swelling in the course of the fibre, or perhaps, by breaking through the cell limits, to form a large droplet outside of the cell.

That the long fibres are in reality portions of the protoplasm, or actual bipolar cells, there can be no doubt. Now and then near the cavity in the section, possibly on account of the maceration which the tissue has undergone, single, isolated cells can be studied, showing the presence not only of a nucleus, but also of long, conical processes at each pole. (Fig. 4, *a*.)

In some of the cells, both in longitudinal and in cross-section, evidences of alterations other than fusion can be made out in the black particles. Thus in some cells there appears to be a breaking up into extremely minute, brownish-black granules, which become more or less irregularly distributed. In other cases changes in a single rod or spindle of the black substance can be easily observed. Peripheral layers or flakes separate off from the main mass, appearing as bluish-gray or slate-colored, swollen, flake-like masses adjacent to a central core of very solid or

homogeneous black substance. Again, such a central core may be entirely wanting, and a few flakes can be seen in a much paler background, the latter being formed in part of the black substance which has gone over into solution. In other places the individual rods or spindles are swollen, and seem to consist of two sorts of substance—one staining black or brownish-black in Weigert-Pal, another very pale, almost colorless substance, which stands out sharply from the ordinary protoplasm of the fibre in which the rod or spindle is contained (Fig. 4, *l*, *m*).

Occasionally one of the rows of rods, dots, or spindles takes a tortuous course inside the straighter process of a bipolar cell, and may even form a spiral inside the protoplasm of the latter.

It is surprising how, in the very finest fibrils studied, the pale substance can be made out in addition to the substance which stains black. If very fine fibrils be studied (processes of very delicate bipolar cells?) one can sometimes make out a marked swelling, showing not infrequently varicosities in its course; this swollen portion of the fibril is made up of what looks like a network of the brownish-black substance, arranged in the form of a mantle, the cavity of the mantle and the meshes of the network of the mantle itself being filled up with a pale, translucent substance. As a rule, however, the appearance is not that of a network, but of a minute number of extremely delicate rods, spindles, or dots. Even in very fine fibrils or processes of bipolar cells these occasionally become separated from one another, but tend to remain arranged in longitudinal rows.

This method of staining with Weigert-Pal permits one to recognize the alteration with the greatest ease in parts of the tissue where only single cells are affected. It is found that the change is present not only about the cavity in the tumor, but here and there in different parts of the growth, and, what is still more important, here and there in the white and gray matter of the spinal cord outside the tumor, even at distances well removed from it. The appearances presented in the latter region are precisely similar in individual instances to those met with in the tumor itself.

Weigert-Pal staining; counter-staining with van Gieson's method. Certain details with regard to the fibres, altered and unaltered, can be better brought out by this mode of preparation. Thus the protoplasm of the bipolar cells stains quite differently in different cells and in different parts of the same cell. The majority of the cells stain only feebly or not at all; but some of the larger swollen and more refractive cells show an affinity for the acid fuchsin staining of a dull red tint. It is especially the periphery of the cells which contain the large fused homogeneous masses of the black substance which takes the acid fuchsin stain. Occasionally these refractive peripheries may assume a bright

red color, almost like that of collagen stained by the same method. Not infrequently between this broad, red periphery and the black mass inside the cell a paler area of protoplasm can be seen.

Whereas the red periphery in some instances appears to be homogeneous in structure, in others it looks as though it were made up of reddish balls or blocks. The contour of the cell may sometimes, accordingly, instead of being perfectly smooth, look slightly jagged, the indentations corresponding to the lines of junction of the constituent balls or blocks.

Staining with Altmann's aniline fuchsin; differentiation with picric acid. The refractive masses which stain black in Weigert-Pal take on a red tint with acid fuchsin alone, and hold it much longer than the rest of the tissue on differentiation with aqueous solution of picric acid. If the differentiation be pushed, however, the masses lose their red color; some of the nuclei of the bipolar cells contain masses which stain reddish or of a magenta tint in the acid fuchsin.

Van Gieson's stain. With this stain the appearances vary a great deal with the degree of picric acid differentiation and with the length of time which has elapsed after the specimen has been stained. In general it may be said that the less the picric acid differentiation the more the refractive bodies retain the acid fuchsin, while in much differentiated specimens they lose their acid fuchsin entirely or almost entirely and look bright yellow. In intermediate stages of differentiation one sees varying amounts of substances which have assumed the red and yellow or yellow-green tint. Again, as time elapses after the preparation of the specimens they gradually grow paler in tint, the acid fuchsin apparently being gradually extracted, and the bodies becoming even more yellow or yellow-green in cast.

A moderate degree of differentiation serves best for high-power studies, since in preparations so made it can be seen that the large fused, homogeneous masses have assumed a yellow tint, while the smaller rods, dots, or spindles may be either yellow, yellowish-red, or altogether red. The protoplasm of the bipolar cells remains almost colorless or slightly pink in the majority of cells. In the larger swollen cells, however, there may be a marked affinity for the acid fuchsin or rather for a mixture of the acid fuchsin and hæmatoxylin, since the cell-bodies stain of a rather dull, dirty, purplish-red tint. Fragmentation of this protoplasm into masses, balls, and clumps is frequently met with.

In some of the better preserved cells a distinct fibrillation can be made out in this protoplasm, and the fibrils can be seen, in longitudinal section, running more or less parallel to the central picric acid mass, while in cross-sections they are observed at the periphery of the picric acid mass, the cross-sections of the fibrils being stained of a darker tint in the acid fuchsin than the rest of the protoplasm. In some cases the

central picric acid mass is surrounded by a layer of smaller picric acid bodies, and outside of these, again, can be seen acid fuchsin bodies. In some places these all seem to be within the protoplasm of a single cell, but in other places the various bodies seem isolated and not contained in a common protoplasm. Whether the latter appearance is due to fragmentation of a common protoplasm or to the simultaneous involvement of a bundle of processes of one or of a number of fine bipolar cells, it is difficult to say. One gets the impression that bundles of fibrils or of processes of bipolar cells are common; sometimes in the centre of such a bundle there is a large fibre, the peripheral elements being much smaller and more delicate. These are met with (1) entirely unaltered; (2) with alteration in the central fibre; (3) with alteration of the central and a portion of the peripheral fibres, or (4) with alteration of all the fibres. It is not impossible that these various fibres, arranged in the form of a bundle, converge to form the protoplasm of a single large fibre. If this really occurs one would conclude that some of the bipolar cells split up at their poles into a number of finer subdivisions—an idea which agrees well with the illustrations of the findings of investigators who have worked with maceration methods.

Staining with iron hæmatoxylin. The substance which stains black in Weigert-Pal preparations and which stains bright yellow in picric acid stains of a slate-gray or blackish-gray color in iron hæmatoxylin. This method is of particular advantage for the study of the nuclein in the bipolar cells.

In looking in the bibliography for references to similar degeneration one is surprised to find how few articles there are which deal with degeneration of glia. Weigert, in his exhaustive monograph, makes the following reference to "granular breaking up":

"The fibres are quite smooth, without granular consistence and without circumscribed swellings and thickenings. This holds, however, only for specimens examined perfectly fresh or after careful hardening. If, on the other hand, a spinal cord be examined which has been cut through when fresh, so that the white substance on the surface has become swollen so as to show the cadaveric swelling of the myelin masses, one can be perfectly sure that in the fibres he will find granular breaking up (or that the fibres will be no longer stainable, etc.). This cadaveric breaking up of the fibres was first described by Frohmann, although Virchow had earlier made the general statement that the neuroglia is destroyed by post-mortem influence.

"The granules met with in cadaveric breaking up are at first small, lying along the long axis of the fibres; when the injury is more marked the granules are larger, small droplets flow together, and the larger drops which have originated in this way lie further apart and irregularly distributed. Finally, they appear to dissolve; at any rate, in

very bad pieces no staining succeeds any longer. The granules of the earlier stages of disintegration also stain with more difficulty than do the normal fibres.

"The varicose neuroglia fibres (cell processes), which many authors (on using Golgi's method) picture and describe, are probably nothing but fibres which have undergone previously the cadaveric alteration.

"How the granular breaking up occurs is questionable. In my previous communication, in the year 1890, I called attention to the fact that cadaveric swelling of the myelin appears to play a rôle in this connection. At any rate, as I then stated, the white substances are those which first show the disintegration. It is conceivable, of course, that the cadaverically softened neuroglia fibres are ruptured by the swelling of the myelin sheaths."

The description of Frohmann referred to by Weigert reads as follows:[1]

"The existence of a finely granular gray-ground substance to the gray matter is asserted with especial emphasis. I have not been able to perceive any trace of such a finely granular substance in a number of very beautiful preparations which I have examined. That it, however, is found sometimes in the gray substance there can be no doubt. Nevertheless, I do not hold it to be a normal constituent of the neuroglia: On the one hand, here, as in the white substance, confusions with fibre cross-sections may slip in, which, where they are closely crowded, lend a granular appearance to the tissue, and in thicker sections and imperfect illumination are with difficulty distinguishable from simple granules; but, on the other hand, not infrequently the fine fibres of the gray substance break up into a number of pale, smooth-contoured white or grayish granules. This occurs especially distinctly where the tissue has been torn, and there one can see, besides the granules, also smaller or larger fragments of fibres which have lost their glistening appearance as well as their fine but definite contours.

"In the continuity of the section the individual fibres are no longer distinctly separable from one another, and with the free granules lend to it a dull, grayish appearance. I hold these alterations to be the product of beginning decomposition—a post-mortem phenomenon which can also frequently be observed in the cortical layer. In favor of this view, speaks, it seems to me, the fact that I met with a finely granular substance most frequently in the ventral and dorsal horn, where the fibres are of great delicacy; while they were not seen at all or were met with but rarely in the dorsal commissure and in the substantia gelatinosa, where the fibres are coarser. Free spherules and spherules not attributable to the breaking up of fibres were seen by me only in preparations containing myelin; they were clear and glistening, occurred only singly

[1] Frohmann, C.: Untersuchungen ueber die normale und pathologische Anatomie des Rückenmarks. Theil I., Jena (1864) S. 49–50.

and scantily, were not stained by carmine, though the larger ones, at least, were colored yellowish with iodine. These must, accordingly, be held to be small myelin spherules."

The similarity of some of the appearances in the case here described to this *körnige Zerfall* of Frohmann and to the descriptions of the process by Weigert is obvious. The fragmentation of the fibres, the formation of varicosities, etc., are striking features in this resemblance. The descriptions of both Frohmann and Weigert, are, however, so meagre that it seems scarcely possible to decide as to the exact relation of the changes in the present case to their *körnige* or *kadaveröse Zerfall*.

The description of glia degeneration which approaches most nearly to that of the case here studied is that of Rosenthal.[1]

Rosenthal had the opportunity of studying a peculiar tumor of the spinal cord associated with syringomyelia. The tissue contained an enormous number of cells of the ependymal type. In it were also typical glia cells and glia fibres. He describes in this case in the close, newly formed glia tissue a peculiar element, abundant and striking in certain parts. This element appears in the form of glistening structures, which assume the shape of small bulbs or twisted sausages, with a thicker and narrower end. The largest of them show a tendency to lamellation, and resemble corpora amylacea, but do not give the typical reaction.

The staining reactions are peculiar. Tissue hardened in Zenker's fluid and stained by the method of van Gieson contains the bodies stained of a brownish-yellow color, sometimes of almost a greenish tint, often with a red contour. In specimens hardened in Müller's fluid they stain bright red by van Gieson's method—quite differently from the haline degeneration of the walls of the vessels. By the method of Weigert-Pal they stain jet black without blue tone. If the decolorization be pushed they stain no longer black, but look dark brown, although they are still sharply marked off from the light brown surrounding tissue. Weigert's glia stain was applied to Zenker preparations and stained the structures blue black or bluish-gray, with a blackish-blue contour.

In Weigert's fibrin stain the masses retain a bright blue color. They are most distinct in iron hæmatoxylin preparations, in which they are stained jet black in the dull gray sections. This reaction, however, is applicable to Zenker preparations only, not to the Müller's fluid preparations. In the latter the iron hæmatoxylin gives results similar to those with the method of Weigert-Pal.

Rosenthal describes the structures, which resemble swollen bulbs and sausages, as being made up in large part of round lumps and very fine

[1] Rosenthal, W.: Ueber eine eigenthümliche mit Syringomylie complicirte Geschwulst des Rückenmarks. Beiträge z. Path. u. path. Anat., Jena, 1898, Band xxiii., S. 111–143.

spherules, which often lie together in rows or groups. In some of the preparations he sees a common contour about the darker staining spherules, and believes that the spherules represent parts of the structures which stain *in toto* in van Gieson's preparations. He finds the structures accumulated particularly about the larger vessels, where, together with undoubted glia fibres, they form a thick ring on the outer surface of the connective-tissue sheath of the vessel.

Curiously enough, Rosenthal could make out no relation between these structures and the cells. He found, however, that they were present in the periphery of the cord outside the tumor, where, after secondary degeneration, there had been glia proliferation. Benda, who, as Rosenthal states, called his attention to these structures, had repeatedly observed these bodies in gliomata, and thought that they represent some pathological new formation or attempt at new formation of myelin sheaths.

Rosenthal, however, comes to the conclusion that they are significant of a form of degeneration of glia fibres in Weigert's sense. In favor of this view he emphasizes the following points:

1. The structures are found only where there has been an over-production of glia.
2. No relation to cell bodies can be made out.
3. They resemble closely in form and arrangement irregularly swollen fibres.
4. They stain by the same methods and in the same color as glia fibres.
5. They have been found in two cases in tumor tissue in which, along with cells and glia fibres, no other element (nerve-fibres, myelin sheaths, connective-tissue) was demonstrable.

Rosenthal designates the process as "*kolbige degeneration*," and thinks that many corpora amylacea belong here, especially those which do not yield the iron reaction. He states that he can find no reference in the literature to structures resembling this degeneration of glia fibres, and suggests that the lack of data is dependent upon the meagre knowledge concerning glia which existed before Weigert's studies.

A comparison of the description of the case now described with that of Rosenthal shows many points of agreement, but some divergence. The staining reactions, the gross form relations, and the general distribution of the bodies are similar in the two cases. In the present case a number of details observable with oil immersion lens have been described which finds no counterpart in Rosenthal's description. A fundamental difference, too, is found in the descriptions as regards the relation to the bodies of cells, whereas Rosenthal states that no relation to cell bodies can be made out; in the tissue from Dr. Hudson's case a very large proportion of the structures are undoubtedly

within the bodies of bipolar cells. Particles of the substance yielding precisely the same staining reactions can be found even within the nuclei of some of the bipolar cells. The data are as yet totally insufficient for the making of any statement with regard to the existence of any constant relation between nuclear function and the appearance of the substance in the protoplasm of the cells or fibres. Glia fibres in Weigert's sense appear to have been present in much greater numbers in Rosenthal's tumor than in the case here described. Unfortunately, the mode of hardening in the present case precluded the application of the glia stain of Weigert. As stated in the description, however, fibres probably to be regarded as glia in Weigert's sense are to be met with, and a portion of these seem to have undergone the change.

The term "kolbige degeneration," as applied by Rosenthal, seems scarcely suitable, as only a portion of the masses resemble a flask in shape, and the alterations in the finer fibres certainly do not fit in with any such designation. Since the alteration is always associated with swelling and the appearance of refractive masses which have specific staining reactions, it is desirable to use some term which will indicate these features. An entirely suitable term I have not been able to find. As I am convinced, however, that the degeneration in Rosenthal's case and in that of Hudson represent identical processes, I would suggest that the change be called at present simply *Degeneratio micans*, or, if preferred, Rosenthal's degeneration, since he first described the specific staining reactions. It is possible, however, that the acquisition of further knowledge will later on permit of a more satisfactory nomenclature.

The difficulty in Rosenthal's case and in that here described in coming to an absolute decision with regard to the nature of the elements met with (processes of cells or glia fibres), and the undoubted presence of enormous numbers of cells in which fibrils do not appear to exist, is in accord with a number of cases which have been reported. In this connection, and with especial reference to the occurrence of transitional forms between cells with simple protoplasmic processes and cells from which glia fibres have become fully differentiated, the paper of Taylor[1] may be consulted with profit. If Taylor is correct in his conclusions it would be tempting to assume that some of the longitudinal rows of particles of the degeneratio micans in the cells in Dr. Hudson's case correspond to the position of differentiating but not yet differentiated fibrils.

[1] Taylor, Edward Wyllys: A Contributian to the Study of Human Neuroglia. Journal of Experimental Medicine, Baltimore, 1897, vol. ii. pp. 611–634.

III.

a. NOTES ON DR. HUDSON'S CASE OF SYRINGOMYELIA. *b.* REGARDING THE LITERATURE AND PATHOLOGY OF SYRINGOMYELIA.

The following description is intended to supplement that given by Dr. Hudson *in extenso* in the previous pages. Dr. Hudson has covered the general anatomical and pathological points so fully that there remain to be added only some details of structure of the tumor. The literature is not treated in an exhaustive manner owing to its volume, which is so great as to exclude it, but especially because it has recently been reviewed in the excellent paper of Hoffmann and the monograph of Schlesinger. The references made, therefore, are of general interest, or refer to cases in which certain of the unusual features met with in this instance have been observed.

The manner of preservation of the tissue and the several modes of staining the sections have been mentioned. In addition good and helpful results have been obtained through the use of Mallory's phosphomolybdate-hæmatoxylin.

It will be possible to give the additional details of structure in general and without reference to the independent sections, as Dr. Hudson has described the latter so fully.

The description of the tumor will refer (*a*) to the cells composing it chiefly; (*b*) to the bloodvessels; (*c*) to the relation of cells to vessels; and (*d*) to the cavities.

The cells of the tumor are not uniformly distributed throughout the mass; they are collected together in masses and in smaller foci. The smaller areas show regularity in that they are collected about small bloodvessels. The preservation of the cells is not all that could be desired, and yet many details can be made out. First, as to form: The cells are oval or more nearly round; sometimes they appear in more irregular forms, and may be said to be pyriform. Very little distinction is possible between cell protoplasm and nucleus, but I attribute this to the staining and, perhaps, mode of preservation. The cells lie close together or they are separated by areas of lighter appearance. Even where they are closely approximated they are separated by intercellular substance. This substance is fibrillated; the fibrils are delicate, straight or slightly curved, or wavy and sharply contoured. The lighter areas are made up of larger numbers of fibres; these being in predominance. They are direct, and come off in groups from the cells, running in nearly parallel rows until they are lost in another group of cells. Where the cells are distributed more irregularly there is an alternation of small foci of cells and areas of fibres, the latter being continued

among the cells. No other kind of intercellular substance is to be made out between the cells.

The relation of the cells and fibres to the bloodvessels to be described is interesting. Two appearances which depend upon degrees of the same condition are met with. In the first the vessel wall is enclosed by a felted mass of the fibres and is removed considerably from the lines of cells. Depending upon the direction of the section of the bloodvessel the fibres proceed to it in a rectangular (transverse) or in a concentric (logitudinal) direction. While the fibres are felted there is no great complication in this arrangement. In the second it is the cells and not the fibres which enclose the vessel wall. The cells here are at least several rows deep, and they form a dense collar about the wall. There is, however, usually, perhaps invariably, an inner, if narrow, line of fibrils between the cells and the wall, just as, by careful focussing, fibrils can be made out between the cells. A very characteristic appearance is obtained when the cells are removed to a somewhat greater distance from the vessel; under these circumstances the vessel is surrounded by lines of fibrils proceeding from the cells, the latter here often presenting a pyriform appearance, and which come together upon or just before the vessel wall. There is little doubt that these cells and fibres are continuous.

The bloodvessels in the tumor are numerous. They are, indeed, much more abundant than seems necessary if their functions were nutritive only. They make up a not inconsiderable part of the mass. Their characters are various; for the most part they present greatly thickened and hyaline walls, and their lumina are small. Blood-corpuscles can be seen in them. Other vessels, with delicate walls and distended with corpuscles, are met with in the same sections. Complete obliteration or reduction of lumen to a cleft-like opening are encountered in the former vessels.

The thickening of the vessel wall affects vessels of all sizes, excluding capillaries. The walls thus altered are quite or nearly homogeneous; only rarely do they show distinct fibrillation, and they are refractive and hyaline; distinction into muscular and adventitial coats is wanting. Within the hyaline walls there is deposited in many cases a granular, bluish sediment in specimens stained in hæmatoxylin, which lies just next the lumen or some distance removed. Its exact nature is more or less conjectural; but it resembles the deposit of lime-salts sometimes seen in large vessels. It is highly probable that there has taken place in these vessels an extensive hyaline and perhaps calcareous degeneration of their walls. A similar degeneration is not met with in the bloodvessels of the remnant of the cord or in the pia mater. In the diseased vessels one of the striking features is the persistence of the vasa vasorum after the thickening has become extreme, and indeed after complete occlusion of the lumen. Occasionally, instead of com

plete homogeneity of the walls a nucleus of elongated form is still present, and now and again globules resembling colloid droplets are made out in the walls.

The Cavities. Two kinds of cavities can be distinguished: (*a*) pre-formed; (*b*) softened. With the softened cavities are to be ranked foci of partial or complete necrosis in which the degenerated elements have not as yet been removed. Certain secondary changes have taken place in some of the softened cavities, chief among which is hemorrhage, although there is evidence of a fibrinoid transformation of portions of the necrotic tissue, or perhaps only of the coagulation of lymph poured into them. Hemorrhages have also occurred in the pre-formed, epithelial-lined cavities.

The pre-formed cavities. Their sizes, number, and location have been stated already. Their walls are composed of neuroglia in which the fibres are very distinct. The fibres form a wide layer just about the periphery of the cavities, thus making up its boundary wall. Very few cells are present in the felt-work of fibres, although many of these are mere prolongations of cells lying some distance removed. This appearance can be compared with the fibrillated layer about the central canal of the cord. Upon this layer of fibres the high epithelium lies. In favorable sections the epithelium investment is almost perfect; in less favorable ones only fragments remain. It is exceedingly probable that in many instances the loss is accidental, and probably took place post-mortem. Where there are slight defects in the epithelial membrane, small bundles of fibres project into the lumen; this, too, I take to be accidental.

When one examines closely the edges of the cavity it is seen that among the fibrils there is contained an irregular globular or coarsely granular material of moderately high refraction. This material is probably a precipitate, and may have come from degenerated neuroglia in this situation. However, other evidences of degeneration are wanting. A few red blood-corpuscles have escaped into this tissue.

As has been described already, hemorrhages have occurred in these cavities; in the sections recent blood-coagula are contained in cavities surrounded by a complete investment of epithelium. The coagula often assume the appearance that suggests congeries of bloodvessels within the cavities; there are artefacts due to inclusion of columns of blood-corpuscles within fibrinous channels. Neuroglia cells and fibres may be incorporated with these channels when disintegration of the walls of the cavities has been caused by or resulted in the hemorrhage.

The softened cavities. Secondary cavities of this nature undoubtedly are present in the sections, but it is not always possible to say positively that any large cavity originated in this way. It is possible that certain of the large cavities, devoid of epithelial lining, with disintegrating walls

or edges, and containing coagula, blood or fibrin only, may represent pre-formed cavities which have suffered disintegration. On the other hand, the sections show now and again lighter or pale areas, which, on close inspection, may be discovered to be centres of disintegration. Where the beginning can be made out it is in masses of fibres rather than in groups of cells that the disorganization commences. Red corpuscles become extravasated; faintly refractive globules appear, fibres break up, and soon only a formless detritus remains. Another appearance that suggests the beginning of cavities is seen about certain bloodvessels (veins?) and consists of a pale, granular coagulation, not unlike coagulated serum, although the material is the coarser granules. In the larger foci remains of bloodvessels with hyaline, thickened walls, which appear to have been obliterated, are present.

From the description given by Dr. Hudson of the gross anatomical character of the pathological condition found in the spinal cord, and from the microscopical features observed, there can be little doubt that the pathological formation must be regarded in the light of a tumor. The occurrence of a circumscribed new growth, displacing and destroying the normal tissues of the cord, leading finally to its complete disintegration, is inconsistent with any other conception.

The microscopical appearances leave no doubt as to the nature of the tumor; it is a glioma. In some respects, however, it is peculiar, for it is exceedingly vascular—indeed, if the growth were a sarcoma one would feel justified, in view of the new formation of bloodvessels which has taken place, in speaking of an angiosarcoma; but what is more peculiar still is the relation between the cells composing the tumor and the bloodvessels. It will be recalled that there is a definite grouping of the former about the latter. The cells themselves are of interest because of their forms. For the moment we may disregard the high epithelium lining the cavities and give attention only to the cells of the tumor proper. These are polymorphous; some are round, some oval, and others pyriform. The last are much commoner than one might suppose from a casual examination, for wherever the elements are separated—*e. g.*, softened areas, breaks, œdema—this form of cell is very numerous. The cells really are more complex than the term employed signifies, for besides nucleus and protoplasm there are processes, one or two in number, which belong to them. The round or oval cells are also provided with processes, but whether they come off from one pole or both poles, or entirely surround them, is not easy to settle. The first appears to be the rule. Between the cells and the fibres there is not, unless degeneration is going on, any demonstrable, definite intercellular substance.

The arrangement of the cells about the bloodvessels in circles, so as to give rise to appearances suggestive of rosettes, seems not to have

been noticed in syringomyelia. It has, however, been observed in gliomata in other regions. I have described a tumor of the retina in which the neuroglia cells grouped themselves in rosettes, not necessarily, however, about bloodvessels (*Johns Hopkins Hospital Bulletin*, 1891). In a glioma of the brain (*Journal of Nervous and Mental Diseases*, May, 1898) I have described a similar condition to that present in the cord in this case. The conceptions expressed in the previous instance regarding the nature of the cells may, it seems to me, be applied in the present one. In order that they may be entirely clear, I will quote from my recent paper the views as expressed by me and which are now held regarding the embryology and histogenesis of neuroglia. (*Ibid.*)

"The cells destined to become glia are derived in the embryo from the medullary plate, and are at first of the same value as the elements which eventually produce nerve-cells. The possibility that cells of other value, leucocytes and endothelial cells, may, at a later period, become interpolated between the elements of ectodermal origin, and, under certain pathological conditions, act as tissue formers, while admitted by so good an authority as Ramon y Cajal, have been shown to be improbable by the researches of Schaffer and v. Lenhossék.

"The glia cells—or, to use the term proposed by Fish in this country and v. Lenhossék in German, astrocytes—take their origin in the lowest and highest vertebrates from the ependyma cells, which are known to belong to the supporting cell structures of the cord. In certain low forms (myxine, amphioxus) the ependyma cells represent the total of the supporting cells, while in the higher forms greater or less numbers of astrocytes supply the chief framework of the organ. In mammals, and especially in man, astrocytes may, it is considered by some, develop from a less highly differentiated cell than ependyma cells, which yield them exclusively in the lower forms. It is proposed to call the intermediate cells (undeveloped forms) astroblasts.

"The several different forms of glia cells, those possessing long processes, those provided with short processes (typical astrocytes), and still others, in which the filaments come off from one or both poles only (brush cells), as well as the true ependyma cells, have all the same ultimate origin. Since Weigert's publication in 1890, and more especially since the appearance of his monograph on neuroglia, much attention has been given to the relation existing between the fibres and the cells in neuroglia.

"The pictures given by the Golgi's silver stain seem to show a close union between processes and cell bodies, and to indicate that the former are mere protoplasmic elongations of the latter. The method of staining introduced by Weigert, and more or less modified by Mallory and Beneke, would seem to necessitate a modification of these views, since by its employment differentiation between fibres and cells in adult neu-

roglia has been rendered possible. According to Weigert, neuroglia, in human beings, consists of cells showing protoplasmic processes only during embryonic life; in the matured or adult condition it is made up of a mixture of cells and fibres, in which the latter so greatly predominate that they are to be regarded as its chief constituent."

Rosenthal (Ziegler's *Beiträge*, Band xxiii. p. 111) has described a case of syringomyelia associated with tumor formation in which the tumor consisted in a number of small cavities, lined with high epithelium, and of fibres and cells shown to be neurogliar in nature. Rosenthal regards the tumor as having originated from ependyma cells, and proposes to call it neuroepithelioma gliomatosum mikrocysticum. The tumor in question presented an adenomatous structure, and was, in his opinion, developed from the epithelium of the neural canal, which was present in several stages of development. This tumor is regarded by Rosenthal as unique; it is practically so only as regards the spinal cord, for it agrees in certain ways with neuroepithelioma of the retina and somewhat less with the ependymal-celled glioma of the brain mentioned.

If we compare the form of cells observed in the glioma of the cord with those met with normally in the developing or adult spinal cord, there is no difficulty in determining much similarity between the ependyma cell, especially that observed in the embryonic state, and many of the cells composing the tumor. Indeed, I should be disposed to regard the tumor as largely made up of such ependymal elements. There is significance also in the fact that the tumors of the central nervous system, thus far described, in which the ependyma cell has been found, show the same tendency to the formation of whorls and to be grouped about bloodvessels.

To come back to the cells lining the pre-formed cavities. These are typical adult ependyma cells. Their relations to the other cells of the tumor roughly are the relations between the cells lining the central canal of the cord and the layer of neuroglia outside. Just as in the normal cord this layer is chiefly fibrillar, the fibres representing prolongations of the high ependymal epithelium and the modified ependyma cells next the canal, which are a part of the supporting framework of the organ, so in the tumor the high epithelium lies upon a fibrillar structure that originates certainly from the ependyma-like cells of the tumor, into which, not improbably, similar fibres derived from the columnar epithelium may pass. According to this view, the tumor under consideration is a glioma of the type described by me under the name of "ependymal-celled glioma."

The relation of the cavities to the tumor and the origin of the high epithelium lining a part of these can be discussed best after considering briefly some of the later views regarding the pathology of syringomyelia.

The oldest and most useful division of cavity formation in the spinal cord is into hydromyelia and syringomyelia. There is, however, not entire unanimity of opinion as to the limits of each. One of the older conceptions regards syringomyelia as a condition in which vertical cavities, either entirely independent of or only accidentally united with the central canal, exist in the spinal cord. The pathogenesis of this cavity formation can be various. In the majority of instances it results from the disintegration of a primary new growth of neuroglia. It has been customary to speak of this new growth as gliosis or gliomatosis, depending upon the extent of the formation and its resemblance to a tumor. Saxer (*Ueber Syringomylie:* Zusammenfassendes Referat, *Cent. f. Pathologie*, 1898, Nos. 1 and 2); Muira (Ziegler's *Beiträge*, 1892, Band xii. p. 118) has attempted a distinction between instances of true tumor formation (glioma) and mere increase in neuroglia. He thinks the cases differ anatomically as well as clinically. However, instances are recorded, as in the case here reported, in which, in the same spinal cord, besides the existence of definite tumors, less circumscribed growths of glia had taken place, and in these cavities had developed. Other cases of this kind have been reported by Marchand and Reisinger, Daxenberger and Rosenblath. (See Saxer, *op. cit.*, p. 16.)

Miura would drop the term "gliomatosis" entirely; the distinctions should be made between glioma, as a circumscribed tumor, and diffuse glioma when the growth is more diffuse or general. The literature contains relatively few cases of cavity formation in the spinal cord which have originated in glioma used in this sense. The great majority of instances have arisen in more diffuse growths—"gliosis" or "central gliosis" of Hoffmann.

The new formation of glia occupies regularly the central part of the cord in the neighborhood of the central canal, and generally its location is behind (dorsal) the canal. This regularity of location is one of the main points of difference as compared with the tumor growths. The new growth takes place in a longitudinal direction, and, in most cases, it is tunnelled by a tubular cavity. The cavity, however, may vary greatly as regards size and form. All transitions have been noted between such a condition as described and instances in which, throughout the whole length of the cavity, very little or no increase in glia can be demonstrated. The usual conception regards the new growth of neuroglia as the primary condition and the cavity as representing a degenerative process.

It is desirable to consider the cause of the primary new growth of neuroglia about the central canal which this theory assumes, and to inquire whether there is any causal relation between the central canal or the central ependyma fibres and the central gliosis. The best answers to these questions which can be given at this time are the views expressed

in the monographs of Hoffmann[1] and Schlesinger.[2] These authors consider the primary condition to be some congenital anomaly which results in the persistence of nests of embryonal tissue behind the central canal, perhaps in the line of closure. Hoffmann regards as of equal importance for the etiology the existence of multiple spinal canals or their "anlage," and the occurrence of large cells, the equivalents of ependyma cells in the posterior commissure in the neighborhood of the posterior longitudinal fissure. According to Hoffmann, the new growth of glia arises from the central canal epithelium or its equivalent in the line of closure or from the "subepithelial epithelioid" cells. Hoffmann regards, therefore, as the principal factors in the production of the pathological condition to which the name syringomyelia is applied, (1) some congenital anomaly of development in the cord, and (2) activity of the epithelium of the central canal.

Schlesinger agrees in the main with Hoffmann's views. He conceives, in addition, that anomalies in the vascular supply are largely responsible for the formation of cavities. He says: "Disease of the vessels plays a rôle co-ordinate with the central gliosis." Schlesinger also discusses the frequency of the occurrence of a lining, partial or complete, of high (central canal) epthelium in the cavites, and he concludes that this is a much more common phenomenon than has been believed heretofore. He would place hydromyelia, with its completely epithelial-lined canal, and syringomyelia, with only, at times, a neuroglia or connective-tissue lining to its cavities, at the two ends of a single anatomical state. Indeed, he goes even further and described cavity formation in previously normal cords as syringomyelia, the cavities in these cases being the result of vascular disease; and he believes that tubular hemorrhages may give rise to a similar condition.

The views of Hoffmann and Schlesinger have emphasized the part played by the central canal epithelium in the production of the central gliosis. Saxer (*op. cit.*, p. 52) also attributes a large rôle to this structure. His views may be summarized as follows: There are positive as well as theoretical grounds for considering the central canal epithelium as capable of taking part in the production of pathological glia formation. The process, however, does not proceed in the manner described by Hoffmann, but it conforms to the processes met with in the embryonic spinal cord. Moreover, Saxer thinks that in the multiplication of the epithelium of the central canal and its equivalent there is produced not only neuroglia, but structures of typical epithelial character, such as that lining clefts and cavities and the foci of epithelial cells in the posterior line of closure. Through this new growth of epithelium there

[1] Deutsche Zeitschr. f. Nervenheilkunde, vol. iii., 1893.
[2] Die Syringomyelie, Vienna, 1895.

may ultimately develop supernumerary or duplicate central canals. Saxer does not think it proven that the central canal epithelium is the essential source of the new tissue, or that, as a rule, the new growth starts from this structure.

Reference has been made to the view entertained by Schlesinger that cavity formation leading to syringomyelia may occur without increase in neuroglia. Müller and Meder (*Zeitschr. f. klin. Med.*, Bd. xxviii.) have encountered a similar condition. In both profound disease of the vessels existed. The irregular and slightly increased amount of neuroglia found by Müller and Meder is considered by them to be of secondary origin. Weigert (*Beiträge z. Kenntniss d. Normalen Menschlichen Neuroglia*, 1895) has brought forward similar cases, and from them he draws the following interesting conclusions (*op. cit.*, p. 156): "Ignorance of the extent of the thickening of the glia about the central canal has given rise to mistakes. It has led to the fable of the softened central gliosis in syringomyelia. The confusion has been increased by confounding gliosis with glioma. The conception of the 'softened central gliosis' involves the idea of an increase in typical, fibrillar neuroglia with softening; but the neuroglia is normally much increased about the central canal, and, indeed, as compared with this form it may be actually diminished in syringomyelia and hydromyelia. On the other hand, one finds extensive glioses, as, for example, in multiple sclerosis; but these do not soften, and, indeed, it has never been proven that true gliosis does soften. In a word, the conception of syringomyelia as softened central gliosis has not the shadow of a probability to support it."

Saxer (Zeigler's *Beiträge*, Band xx.) has attempted to answer this criticism, and he has drawn attention to the fact (1) that the process of softening has been observed and described step by step, and (2) that many cases with great increase in glia, excluded from being of secondary growth, have been encountered. However, it is admitted that cases to which Weigert's description applies do exist.

These points have been developed with some fulness, inasmuch as the case described in this paper covers two of the disputed questions: (1) Beginning and advanced softening were observed in the pathological glia; and (2) the extent of character of the pathological new growth proves it to have been of primary origin.

The present case is also of theoretical interest in respect to the light thrown by it upon the question of the participation of central canal epithelium in the production of the new growth of glia. All recent writers have dwelt more or less on this feature; apparently only Saxer has regarded a return to embryonic conditions in the epithelium as probable. Although Saxer takes pains not to overemphasize the theory of congenital anomaly in predisposing or leading to the production of new tissue, yet his view involves some such condition. Upon theoretical

grounds alone V. Lenhossék (*Der feinere Bau des Nervensystems in Lichte Neuester Forschungen*, 2 auflage, p. 176–248) has regarded abnormalities in development as playing a large part; and Hoffmann believed he had found the misplaced elements which in development gave rise to the new tissue. If the views expressed in this paper are correct, the new tissue, in the case here given, is made up of cells having the value of central canal epithelium, but existing in an embryonic rather than in a fully developed state. Further, the arrangement of the cells is highly suggestive of that of the embryonic ependyma, the bloodvessels in this instance supplying the place of the central canal of the cord.

Without laying too much stress on the probability of the view expressed by Saxer, it is yet worth while to mention that as conceived by him, along with the products of embryonal ependyma, those of the developed tissue are afforded by the high epithelium lining many of the cavities.

Finally, it may be well to add just a word on the mooted question as to whether the new tissue in this case is to be regarded as a tumor. The lines between simple new growth of tissue and that growth that constitutes for us "tumor" is not sharply drawn. We regard, however, an independent formation of tissue, not arising merely as a protective or supporting structure, or in response to the action of some known irritant (actinomyces for example), as a tumor. Moreover, tumors often differ from simple tissue growth because they occur and persist in a state of development foreign to the tissues after a certain period (sarcoma). While granulation tissue at a certain stage may resemble sarcoma, it will sooner or later cease to do so, because it tends to change progressively into adult tissue. Fixity in an abnormal state of development is one differential point. Apparently this is the condition in the process described in the spinal cord. There has been a great increase in neuroglia; but the cells are not the type of adult, developed, neuroglia cells, nor are a part embryonic and another part certainly adult cells, if we exclude the high epithelium lining the cavities. The tumor cells proper are all embryonic and of the type of early ependymal cells. The circumscription of the growth, its evidently primary character, the state of development of its composing cells, would in other situations, at least, if the same kind of conditions could be met with, lead to the conclusion of tumor formation. M. Allen Starr[1] has recently reviewed the literature concerning this consideration as well as some other questions concerning syringomyelia.

[1] Journal of Nervous and Mental Disease, January, 1897.

DESCRIPTION OF PLATES.

PLATE I.

The drawing shows the position within the spinal cord of the new growth of glia and its extent; it also indicates the levels of the several sections and their chief characteristics. The letters E.C. indicate the epithelial cavities. T. is the tumor.

PLATE II.

FIG. 1 corresponds to Plate I., Section 1. Central growth of glia developed within the gray matter of the cord, chiefly within the posterior horns, which are entirely destroyed. Anterior horns partially preserved. *a* and *b*. Epithelial-lined cavities. Weigert, Pal, and van Gieson's method. Magnified 6 times.

FIG. 2 corresponds to Plate I., Section 4. The new growth is somewhat more extensive, and, while occupying the entire posterior segment of the cord, it also encroaches upon the anterior white matter. The central zone shows rarefaction. *a b c*. Epithelial-lined cavities. Magnified 6 times.

FIG. 3 corresponds with Plate I., Section 5. Except for the large number of epithelial-lined cavities, *a b c d e f*, it is similar to Fig. 2. Magnified 6 times.

PLATE III.

FIG. 1 corresponds with Plate I., Section 6. Two foci (stems) of tumor developed centrally in the cord, but posterior to the anterior commissure. The position of the central canal is indicated by *c*. In the larger focus an epithelial-lined cavity, in the smaller, a degenerative one, are shown. Magnified 6 times.

PLATE IV.

FIG. 1. Portion of Section 4, magnified 500 times. This drawing is from a softened area into which hemorrhage has taken place. It shows fragments of fibres, naked nuclei, and free red blood-corpuscles. There are independent cells and fibres, probably due to a degenerative process. Stained after Van Gieson's method.

FIG. 2. Portion of Plate I., Section 3, magnified 100 times. Projecting folds, resembling Grecian columns, covered with cylindrical epithelium, are shown. The folds are composed of rosettes of polyform cells, the similarity to ependyma-cells being evident. Bloodvessels with much thickened walls and others with normal walls are present. The rosettes are developed about small bloodvessels. Stained in hæmatoxylin and eosin.

ADDITIONAL FIGURES.

Plate III., Fig. 2. Section through half of stem of new growth, showing part of cavity and distribution of the larger masses of glistening degeneration (Degeneratio micans). Müller's fluid, hardening, celloidin section unstained, mounted in salty glycerin, magnification of 10 diameters. The branch of the cavity marked *x* corresponds to the portion seen under higher power in Fig. 3.

Plate III., Fig. 3. Higher magnification of a part of the same preparation represented in Fig. 2.

c. Bloodvessels. The masses of the glistening substance assume various forms. A large number of pale swollen fibrils containing none of the refractive substance are indicated. Near the central cavity the coagulated albumin is seen. Magnification of 62 diameters (Zeiss, Compens. Oc. 4, Apochr. Obj 16 mm.).

Plate III., Fig. 4. Series of drawings representing elements selected from a Weigert-Pal preparation of the tissues pictured in Figs. 2 and 3; magnification of 500 diameters (Zeiss Compens. Oc. 4, Apochr. Obj. Oil imm. 2 0 mm.).

a. Parts of two swollen bipolar cells met with in one field of the microscope. These two cells do not contain the glistening substance. The nucleus is in both placed excentrically, this being obvious in the one cell seen "in profile."

b. Part of long bipolar cell in large part converted into the glistening substance, here stained black. At the thick extremity is a drop of protoplasm showing none of the Degeneratio micans.

c. Part of a swollen bipolar cell showing a black core with peripheral, nearly parallel, rows of dots and rods of the black substance.

d Part of a bipolar cell showing rows of drops and rods, as well as several large drops of the blackened substance. A few very pale areas are visible in the protoplasm.

e. Part of bipolar cell showing central core of substance stained black, which at one end of the figure is resolved into a bundle of parallel rows of black dots and rods. There is a relatively large amount of swollen rather refractive protoplasm peripherally placed, which is free from Degeneratio micans.

f. A small bundle of interrupted black lines of the stained glistening substance embedded apparently in a common ground mass of protoplasm,

g. A complex of sections of fibres of various sizes running in different directions. Fusiform masses of the black substance distinctly visible in some of them.

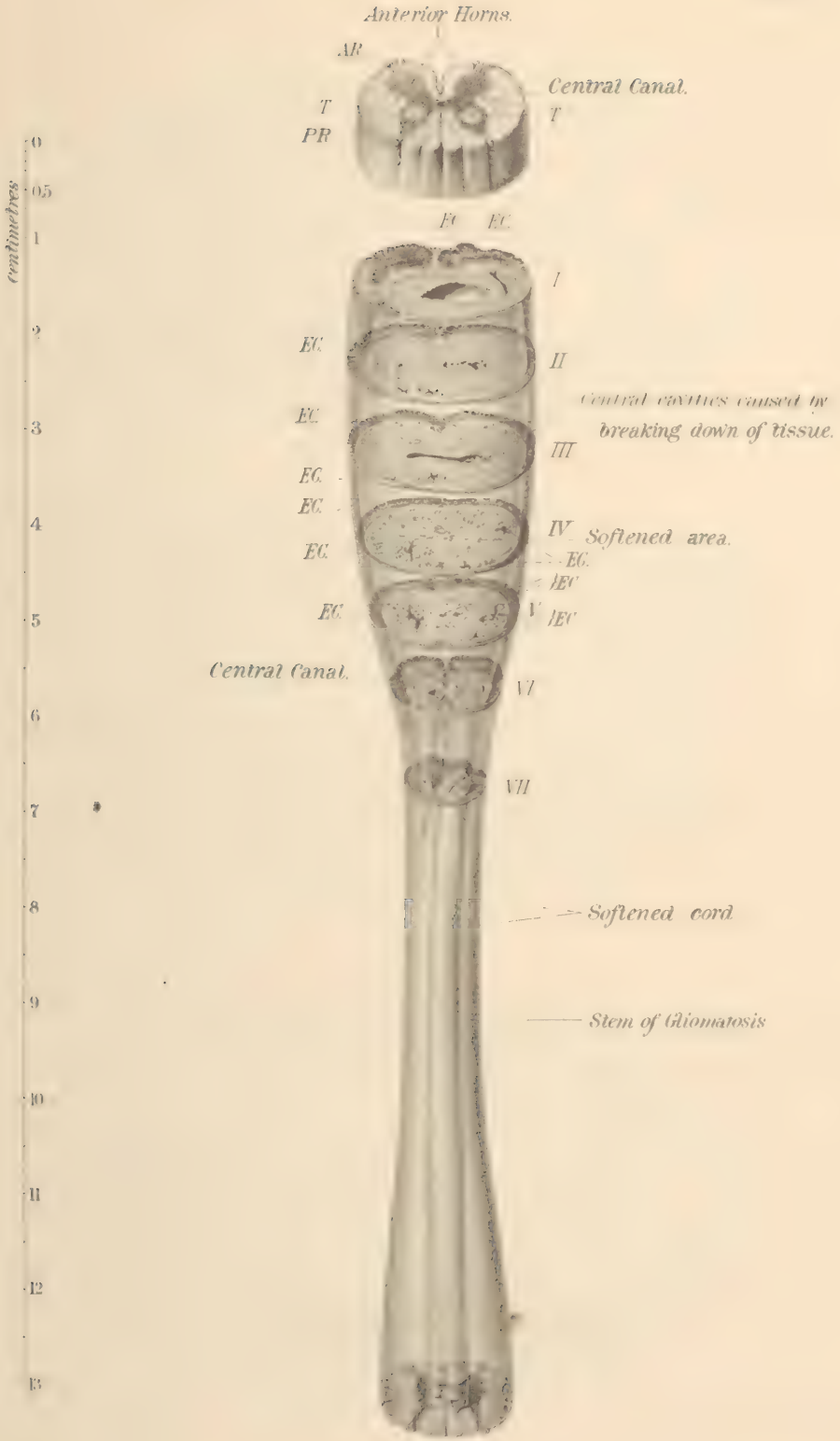
h. Cross section of a rather large bipolar cell showing transverse sections of the longitudinal rows of masses of the blackened Degeneratio micans.

k. Large refractive mass containing particles of the blackened glistening substance. The protoplasm has apparently "run" into this form.

l, m. Sections of swollen bipolar cells containing sections of pale masses. Inside the latter are seen irregularly distributed droplets of the blackened glistening substance.

n. Two very fine fibres, both taken from a part in which all the elements in the tissue are swollen. One of the fibres is free from, the other contains, the substance which stains black in Weigert-Pal.

o A rather fine fibre, showing fragments of the blackened substance. The upper thickened end of the fibre is seen in cross sections and on the cut surface is seen a central core, which consists of a homogeneous fused mass of the blackened glistening substance.



Max Brödel, del.

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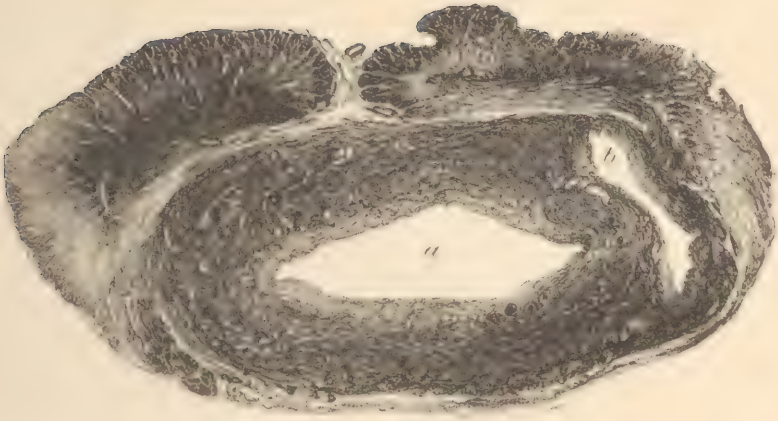

Fig. 1.

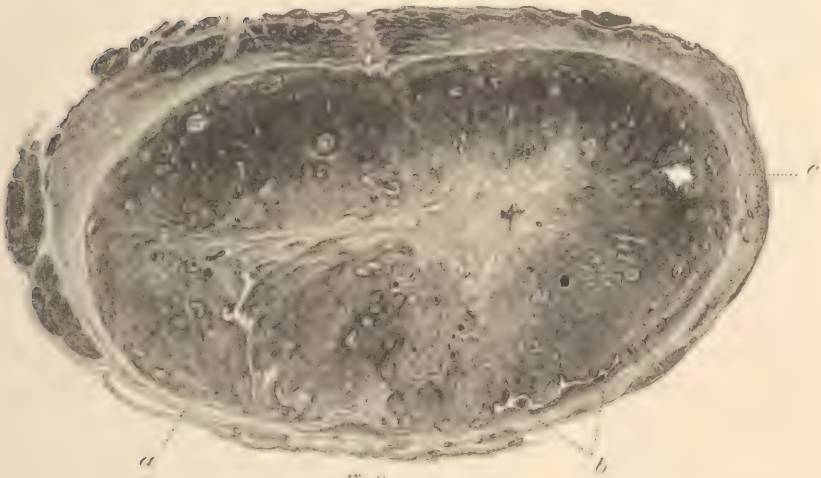

Fig. 2.

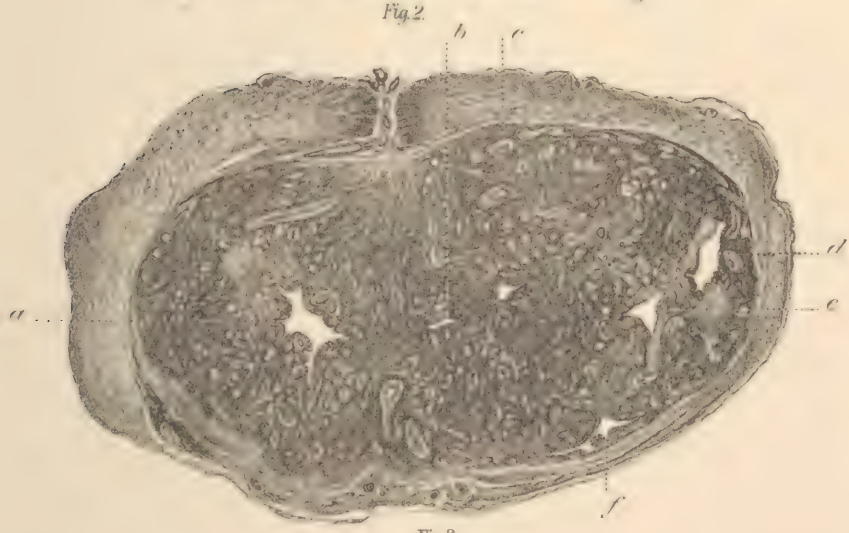

Fig. 3.

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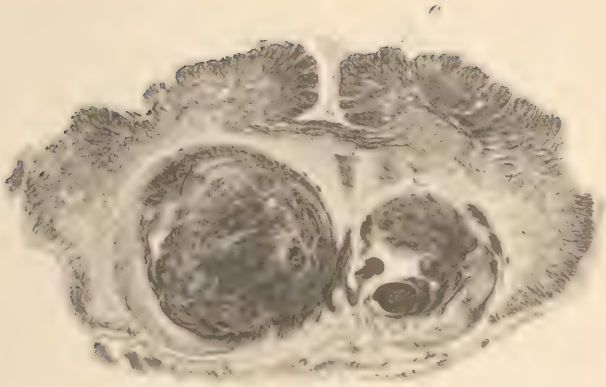

Fig. 1.

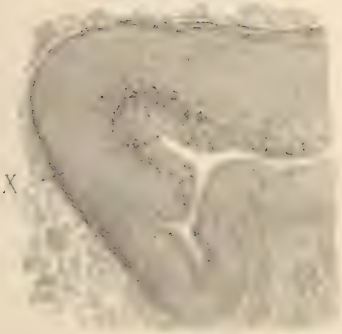

Fig. 2. 1 x 10

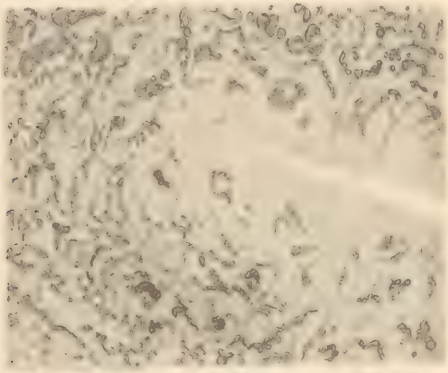

Fig. 3. 1 x 62

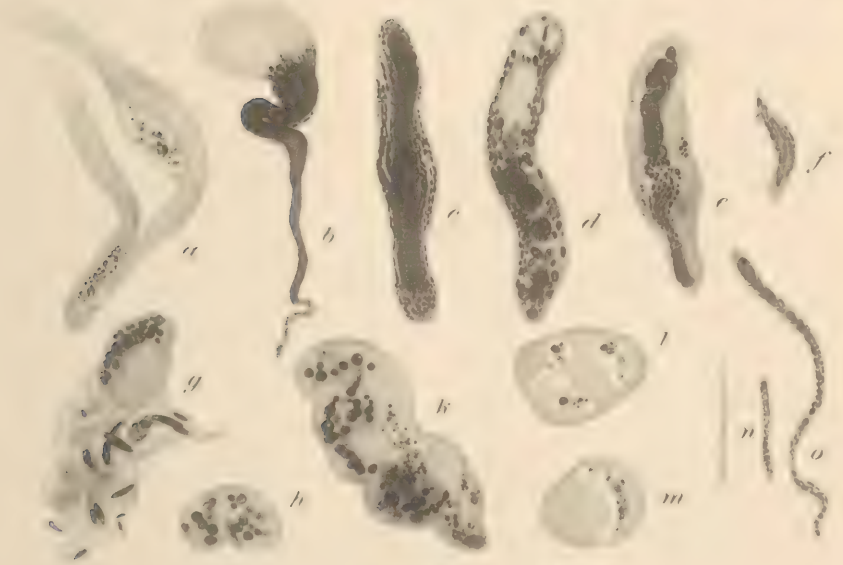

Fig. 4. 1 x 500

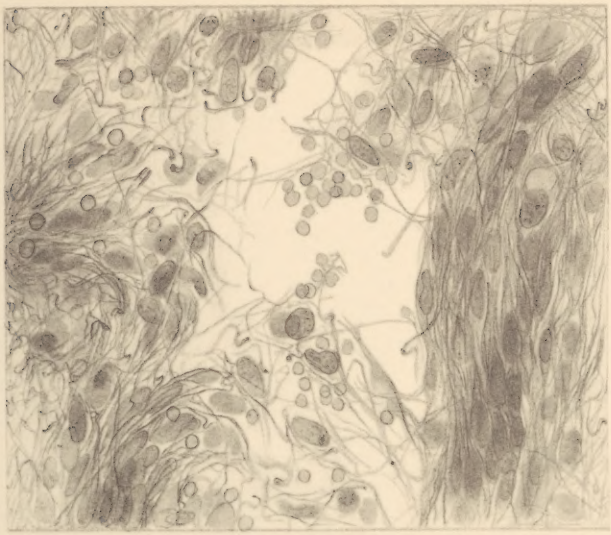

Fig. 1. *1 x 500*

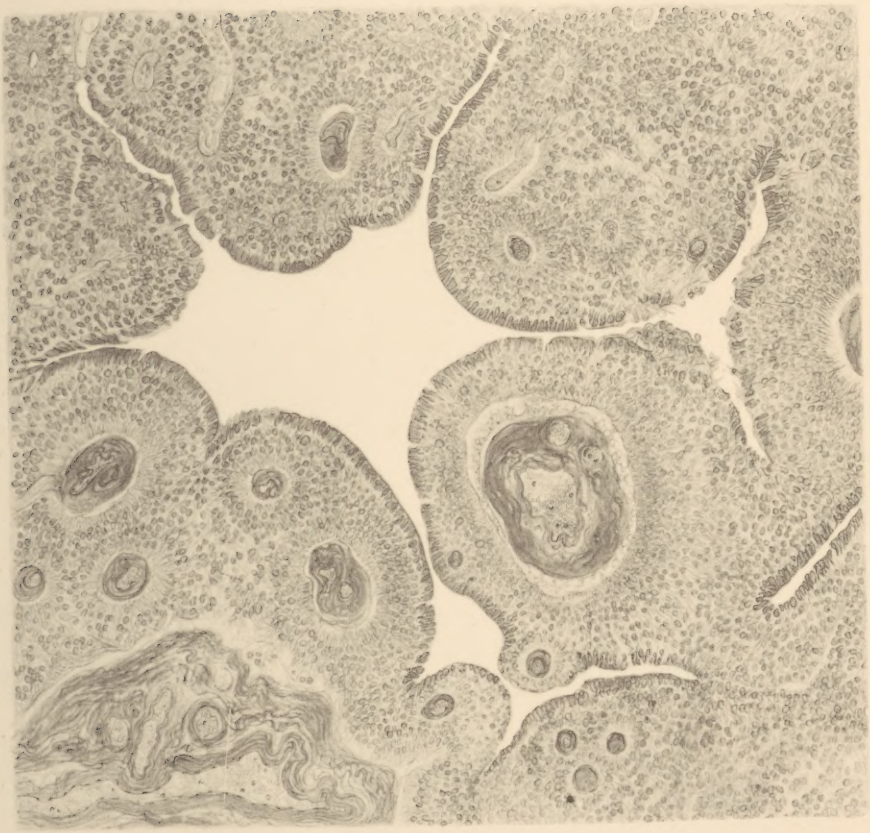

Fig. 2. *1 x 100*

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